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Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:ssspta1642cxy

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08  "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
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 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:54:33 ON 16 SEP 2002

=> file medline, cancerlit, biosis, confsci, embase, uspatfull
COST IN U.S. DOLLARS                                 SINCE FILE     TOTAL
                                                          ENTRY   SESSION
FULL ESTIMATED COST                                        0.21      0.21

FILE 'MEDLINE' ENTERED AT 15:54:59 ON 16 SEP 2002

FILE 'CANCERLIT' ENTERED AT 15:54:59 ON 16 SEP 2002

FILE 'BIOSIS' ENTERED AT 15:54:59 ON 16 SEP 2002
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FILE 'USPATFULL' ENTERED AT 15:54:59 ON 16 SEP 2002
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=> s polyclon? (a) antibod? and librar?
L1        10687 POLYCLON? (A) ANTIBOD? AND LIBRAR?

=> s l1 and expression(a)vector
L2         7077 L1 AND EXPRESSION(A) VECTOR

=> dup rem l2
PROCESSING IS APPROXIMATELY  20% COMPLETE FOR L2
PROCESSING IS APPROXIMATELY  40% COMPLETE FOR L2
PROCESSING IS APPROXIMATELY  59% COMPLETE FOR L2
PROCESSING IS APPROXIMATELY  76% COMPLETE FOR L2
PROCESSING IS APPROXIMATELY  94% COMPLETE FOR L2
PROCESSING COMPLETED FOR L2
L3          6978 DUP REM L2 (99 DUPLICATES REMOVED)

=> d his

     (FILE 'HOME' ENTERED AT 15:54:33 ON 16 SEP 2002)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
     15:54:59 ON 16 SEP 2002
L1        10687 S POLYCLON? (A) ANTIBOD? AND LIBRAR?
L2          7077 S L1 AND EXPRESSION(A)VECTOR
L3          6978 DUP REM L2 (99 DUPLICATES REMOVED)

=> s variable (a) chain and l3
COMMAND INTERRUPTED
REENTER FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL'
AND TRY AGAIN, OR ENTER '?' FOR MORE INFORMATION.
QUERY PROCESSING INTERRUPTED
The system was temporarily unable to process your query.  If this
message appears repeatedly, please notify the Help Desk.  Enter "HELP
STN" for information on contacting the nearest STN Help Desk by
telephone or via SEND in the STNMAIL file.

=> file medline, cacnerlit, biosis, confsci, embase, uspatfull
'CACNERLIT' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
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accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):cancerlit
COST IN U.S. DOLLARS                              SINCE FILE     TOTAL
                                                       ENTRY   SESSION
FULL ESTIMATED COST                                    16.93     17.14

FILE 'MEDLINE' ENTERED AT 16:02:49 ON 16 SEP 2002

FILE 'CANCERLIT' ENTERED AT 16:02:49 ON 16 SEP 2002

FILE 'BIOSIS' ENTERED AT 16:02:49 ON 16 SEP 2002
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=> d his

     (FILE 'HOME' ENTERED AT 15:54:33 ON 16 SEP 2002)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
     15:54:59 ON 16 SEP 2002
L1        10687 S POLYCLON? (A) ANTIBOD? AND LIBRAR?
L2         7077 S L1 AND EXPRESSION(A)VECTOR
L3         6978 DUP REM L2 (99 DUPLICATES REMOVED)
     FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
     16:02:49 ON 16 SEP 2002

=> s l3 and variable(a)chain
QUERY PROCESSING INTERRUPTED
The system was temporarily unable to process your query.  If this
message appears repeatedly, please notify the Help Desk.  Enter "HELP
STN" for information on contacting the nearest STN Help Desk by
telephone or via SEND in the STNMAIL file.

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                              SINCE FILE     TOTAL
                                                       ENTRY   SESSION
FULL ESTIMATED COST                                     8.15     25.29

STN INTERNATIONAL LOGOFF AT 16:06:10 ON 16 SEP 2002
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Welcome to STN International!  Enter x:x

LOGINID:sssptal642cxy

PASSWORD:
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FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002

=> file medline, cancerlit, biosis, confsci, embase, uspatfull
COST IN U.S. DOLLARS                             SINCE FILE     TOTAL
                                                      ENTRY   SESSION
FULL ESTIMATED COST                                    0.21      0.21

FILE 'MEDLINE' ENTERED AT 12:23:48 ON 26 SEP 2002

FILE 'CANCERLIT' ENTERED AT 12:23:48 ON 26 SEP 2002

FILE 'BIOSIS' ENTERED AT 12:23:48 ON 26 SEP 2002
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=> s antibod? and librar?
L1      41608 ANTIBOD? AND LIBRAR?

=> s polyclona?
L2     137092 POLYCLONA?

=> s l2 and l1
L3      15758 L2 AND L1

=> s l3 and phage?
L4       9841 L3 AND PHAGE?

=> s l4 not py=> 1994
'1994' NOT A VALID FIELD CODE
   5 FILES SEARCHED...
L5        414 L4 NOT PY=> 1994

=> dup rem
ENTER L# LIST OR (END):l5
PROCESSING COMPLETED FOR L5
L6          339 DUP REM L5 (75 DUPLICATES REMOVED)

=> d l6 1-50

L6   ANSWER 1 OF 339  USPATFULL
AN     93:109185  USPATFULL
TI     cDNA coding for carcinoembryonic antigen (CEA)
IN     Barnett, Thomas R., East Haven, CT, United States
       Elting, James J., Madison, CT, United States
       Kamarck, Michael E., Bethany, CT, United States
PA     Molecular Diagnostics, Inc., West Haven, CT, United States (U.S.
       corporation)
PI     US 5274087              19931228
AI     US 1992-876821          19920429 (7)
RLI    Continuation of Ser. No. US 1988-231741, filed on 12 Aug 1988, now
       abandoned which is a continuation-in-part of Ser. No. US 1987-60031,
       filed on 19 Jun 1987, now abandoned which is a continuation-in-part of
       Ser. No. US 1987-16683, filed on 19 Feb 1987, now abandoned which is a
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        continuation-in-part of Ser. No. US 1986-896361, filed on 13 Aug 1986,
        now abandoned
DT      Utility
FS      Granted
LN.CNT  1207
INCL    INCLM: 536/023.500
        INCLS: 435/006.000; 435/172.300; 435/320.100; 536/023.500; 536/024.300;
               536/024.310; 935/011.000; 935/027.000
NCL     NCLM:  536/023.500
        NCLS:  435/006.000; 435/320.100; 536/024.300; 536/024.310
IC      [5]
        ICM: C07H015-12
        ICS: C07H021-04; C12N015-00
EXF     435/91; 435/172.3; 435/240.1; 435/240.4; 435/252.3; 435/252.33;
        435/254.34; 435/6; 435/320.1; 536/27; 536/24.3; 536/24.31; 536/24.5;
        935/11; 935/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 2 OF 339  USPATFULL
AN      93:108990  USPATFULL
TI      Gamma-iterferon-leukotoxin gene fusions and uses thereof
IN      Potter, Andrew, Saskatoon, Canada
        Campos, Manuel, Saskatoon, Canada
        Hughes, Huw P. A., Saskatoon, Canada
PA      University of Saskatchewan, Saskatoon, Canada (non-U.S. corporation)
        Ciba-Geigy Canada, Ltd., Saskatoon, Canada (non-U.S. corporation)
PI      US 5273889              19931228
AI      US 1991-777715          19911016 (7)
RLI     Continuation-in-part of Ser. No. US 1990-571301, filed on 22 Aug 1990
DT      Utility
FS      Granted
LN.CNT  1727
INCL    INCLM: 435/069.510
        INCLS: 435/069.500; 435/069.520; 435/069.700; 435/172.300; 435/243.000;
               435/252.300; 435/320.100; 435/811.000; 536/023.100
NCL     NCLM:  435/069.510
        NCLS:  435/069.500; 435/069.520; 435/069.700; 435/243.000; 435/252.300;
               435/320.100; 435/811.000; 536/023.100
IC      [5]
        ICM: C12N015-23
        ICS: C12N015-19; C07H015-12
EXF     435/69.5; 435/69.51; 435/69.52; 435/69.7; 435/252.3; 435/243; 435/172.3;
        435/320.1; 435/81; 536/27; 536/23.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 3 OF 339  USPATFULL
AN      93:108986  USPATFULL
TI      Polypetides, antigens or vaccines protective against babesiosis
IN      Gale, Kevin G., Brisbane, Australia
        Waltisbuhl, David J., Queensland, Australia
        Wright, Ian G., Brisbane, Australia
        Goodger, Brian V., New South Wales, Australia
PA      Commonwealth Scientific & Industrial, United States (non-U.S.
        corporation)
PI      US 5273884              19931228
AI      US 1990-470284          19900125 (7)
PRAI    AU 1989-2427            19890125
        AU 1989-7722            19891116
DT      Utility
FS      Granted
LN.CNT  1771
INCL    INCLM: 435/007.100
        INCLS: 424/088.000; 435/007.220; 435/069.100; 530/388.100; 530/388.600;
               530/350.000; 536/023.100
NCL     NCLM:  424/191.100
        NCLS:  424/266.100; 424/270.100; 435/007.220; 435/069.100; 530/350.000;
               530/388.100; 530/388.600; 536/023.100
IC      [5]
        ICM: G01N033-53
        ICS: C07K015-28; A61K039-00; C07H021-02
EXF     435/6; 435/7.1; 435/7.2; 435/69.1; 435/71.1; 435/71.2; 435/; 435/172.1;
        435/172.2; 435/172.3; 435/240.26; 435/240.27; 435/252.3; 435/252.33;
        435/7.22; 436/501; 436/519; 436/548; 436/63; 530/387; 530/809; 536/26;
        536/27; 536/28; 536/29; 536/23.1; 935/65; 935/95; 935/102; 935/106;
        424/88
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 4 OF 339  USPATFULL
AN      93:108848  USPATFULL
TI      Bacillus thuringiensis isolates active against phthiraptera pests
IN      Payne, Jewel M., San Diego, CA, United States
        Hickle, Leslie A., San Diego, CA, United States
PA      Mycogen Corporation, San Diego, CA, United States (U.S. corporation)
PI      US 5273746              19931228
AI      US 1992-828788          19920129 (7)
DT      Utility
FS      Granted
LN.CNT  1775
INCL    INCLM: 424/093.000L
        INCLS: 435/252.500; 435/252.310; 536/023.710; 514/002.000
NCL     NCLM:  424/093.461
        NCLS:  424/093.200; 435/252.310; 435/252.500; 514/002.000; 536/023.710
IC      [5]
        ICM: A01N063-04
        ICS: A01N037-18; C07H021-04
EXF     424/93L; 424/DIG.10; 435/252.31; 435/252.5; 514/2; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 5 OF 339  USPATFULL
AN      93:107133  USPATFULL
TI      DNA sequences encoding vascular cell adhesion molecules (VCAMS)
IN      Hession, Catherine A., South Weymouth, MA, United States
        Lobb, Roy R., Westwood, MA, United States
        Goelz, Susan E., Winchester, MA, United States
        Osborn, Laurelee, Brighton, MA, United States
        Benjamin, Christopher D., Beverly, MA, United States
        Rosa, Margaret D., Winchester, MA, United States
PA      Biogen, Inc., Cambridge, MA, United States (U.S. corporation)
PI      US 5272263              19931221
AI      US 1989-452675          19891218 (7)
RLI     Continuation-in-part of Ser. No. US 1989-359516, filed on 1 Jun 1989,
        now abandoned which is a continuation-in-part of Ser. No. US
        1989-345151, filed on 28 Apr 1989
DT      Utility
FS      Granted
LN.CNT  2440
INCL    INCLM: 536/023.500
        INCLS: 530/380.000; 435/069.600; 435/320.100
NCL     NCLM:  536/023.500
        NCLS:  435/069.600; 435/320.100; 530/380.000
IC      [5]
        ICM: C07K013-00
        ICS: C12N015-00; C12P021-06
EXF     435/69.1; 435/69.9; 435/320.1; 530/380; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 6 OF 339  USPATFULL
AN      93:106950  USPATFULL
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TI     CDNA encoding the type I iodothyronine 5'deiodinase
IN     Larsen, P. Reed, Brookline, MA, United States
       Berry, Marla J., Brighton, MA, United States
PA     Brigham and Women's Hospital, Boston, MA, United States (U.S.
       corporation)
PI     US 5272078                19931221
AI     US 1992-828790            19920129 (7)
RLI    Continuation-in-part of Ser. No. US 1991-757024, filed on 3 Sep 1991,
       now abandoned which is a continuation-in-part of Ser. No. US
       1991-647657, filed on 29 Jan 1991, now abandoned
DT     Utility
FS     Granted
LN.CNT 2500
INCL   INCLM: 435/189.000
       INCLS: 435/069.100; 435/172.100; 435/252.300; 435/320.100; 536/023.200;
              536/024.100; 935/009.000; 935/011.000; 935/022.000; 935/044.000;
              935/066.000; 935/079.000
NCL    NCLM:  435/189.000
       NCLS:  435/069.100; 435/252.300; 435/320.100; 536/023.200; 536/024.100
IC     [5]
       ICM: G12N015-53
       ICS: G12N015-11; G12N015-63; C12P021-00
EXF    435/69.1; 435/252.3; 435/320.1; 435/187; 536/27; 536/23.2; 536/24.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 7 OF 339  USPATFULL
AN     93:105101  USPATFULL
TI     Nucleic acids encoding fragments of hematopoietic stem cell receptor
       flk-2
IN     Lemischka, Ihor R., Princeton, NJ, United States
PA     The Trustees of Princeton University, Princeton, NJ, United States (U.S.
       corporation)
PI     US 5270458                19931214
AI     US 1992-977451            19921119 (7)
RLI    Continuation-in-part of Ser. No. US 1992-975049, filed on 12 Nov 1992
       which is a continuation-in-part of Ser. No. US 1992-906397, filed on 26
       Jun 1992 which is a continuation-in-part of Ser. No. US 1991-813593,
       filed on 24 Dec 1991, now patented, Pat. No. US 5185438 which is a
       continuation-in-part of Ser. No. US 1991-793065, filed on 15 Nov 1991,
       now abandoned which is a continuation-in-part of Ser. No. US
       1991-728913, filed on 28 Jun 1991, now abandoned which is a
       continuation-in-part of Ser. No. US 1991-679666, filed on 2 Apr 1991,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 1919
INCL   INCLM: 536/023.500
       INCLS: 435/069.100; 435/320.100; 530/350.000; 530/403.000
NCL    NCLM:  536/023.500
       NCLS:  435/069.100; 435/320.100; 530/350.000; 530/403.000
IC     [5]
       ICM: C07H021-00
EXF    536/23.5; 530/350; 530/387.1; 530/846; 435/240.2; 435/69.1; 435/172.1;
       435/320.1; 514/2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 8 OF 339  USPATFULL
AN     93:105095  USPATFULL
TI     Pure glia maturation factor
IN     Lim, Ramon, Iowa City, IA, United States
       Kaplan, Ruth, West Chester, PA, United States
       Jaye, Michael, Glenside, PA, United States
PA     Rhone-Poulenc Rorer Pharmaceuticals Inc., Collegeville, PA, United
       States (U.S. corporation)
PI     US 5270452                19931214
AI     US 1991-785185            19911031 (7)
RLI    Continuation of Ser. No. US 1991-692772, filed on 26 Apr 1991, now
       abandoned which is a continuation of Ser. No. US 1988-276847, filed on
       28 Nov 1988, now abandoned
DT     Utility
FS     Granted
LN.CNT 506
INCL   INCLM: 530/399.000
       INCLS: 530/350.000; 435/172.300; 435/252.300; 435/320.100; 435/069.100
NCL    NCLM:  530/399.000
       NCLS:  435/069.100; 435/252.300; 435/320.100; 435/466.000; 435/483.000;
              435/485.000; 435/488.000; 530/350.000
IC     [5]
       ICM: C07K013-00
       ICS: C12P021-02; C12N015-00
EXF    435/172.3; 435/69.1; 530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 9 OF 339  USPATFULL
AN     93:104845  USPATFULL
TI     Human mannose-binding protein
IN     Ezekowitz, Raymond A. B., Boston, MA, United States
PA     The Children's Medical Center Corporation, Boston, MA, United States
       (U.S. corporation)
PI     US 5270199                19931214
AI     US 1992-831619            19920206 (7)
RLI    Continuation of Ser. No. US 1989-417822, filed on 5 Oct 1989 which is a
       continuation-in-part of Ser. No. US 1987-87628, filed on 20 Aug 1987,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 668
INCL   INCLM: 435/240.200
       INCLS: 435/069.100; 435/172.300; 435/320.100; 435/235.100; 435/252.300;
              435/252.330; 435/254.110; 435/254.200; 536/023.400; 536/023.500;
              530/350.000; 935/018.000; 935/027.000; 935/032.000; 935/034.000;
              935/038.000; 935/055.000; 935/062.000; 935/070.000; 935/072.000
NCL    NCLM:  435/372.100
       NCLS:  435/069.100; 435/235.100; 435/252.300; 435/252.330; 435/254.110;
              435/254.200; 435/320.100; 530/350.000; 536/023.400; 536/023.500
IC     [5]
       ICM: C12N005-00
       ICS: C12N015-00; C12N007-00; C12N001-21; C12N001-16; C12N001-18;
       C12P021-02; C12P019-34; C02K003-00; C07H015-12
EXF    435/69.1; 435/91; 435/172.3; 435/235.1; 435/320.1; 435/240.2; 435/252.3;
       435/252.33; 435/255; 435/256; 536/27; 530/350; 535/18; 535/27; 535/32;
       535/34; 535/38; 535/55; 535/62; 535/70; 535/72
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 10 OF 339  USPATFULL
AN     93:102938  USPATFULL
TI     Overexpression of phytochrome in transgenic plants
IN     Hershey, Howard P., West Chester, PA, United States
       Keller, Janis M., Wilmington, DE, United States
PA     E. I. Du Pont de Nemours and Company, Wilmington, DE, United States
       (U.S. corporation)
PI     US 5268526                19931207
AI     US 1988-284422            19881214 (7)
RLI    Continuation-in-part of Ser. No. US 1988-226344, filed on 29 Jul 1988,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 1928
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INCL    INCLM: 800/205.000
        INCLS: 800/255.000; 800/DIG.009; 435/320.100; 935/035.000; 935/067.000
NCL     NCLM:  800/298.000
        NCLS:  435/320.100; 800/305.000; 800/306.000; 800/307.000; 800/310.000;
               800/311.000; 800/312.000; 800/313.000; 800/314.000; 800/317.000;
               800/317.100; 800/317.200; 800/317.300; 800/317.400; 800/318.000;
               800/323.000; 800/323.100; 800/323.200; 800/323.300
IC      [5]
        ICM: A01H004-00
        ICS: C12N015-29
EXF     800/1; 800/200; 800/205; 800/250; 800/255; 800/DIG.9; 435/68; 435/172.1;
        435/172.3; 435/320.1; 435/69.1; 935/9; 935/10; 935/30; 935/35; 935/47;
        935/64; 935/67; 047/58
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 11 OF 339  USPATFULL
AN      93:102708  USPATFULL
TI      Mammalian adipocyte protein p154, nucleic acids coding therefor and uses
        thereof
IN      Serrero, Ginette, Lake Placid, NY, United States
PA      W. Alton Jones Cell Science Center, Inc., Lake Placid, NY, United States
        (U.S. corporation)
PI      US 5268295              19931207
AI      US 1991-708038          19910531 (7)
DT      Utility
FS      Granted
LN.CNT 2018
INCL    INCLM: 435/252.300
        INCLS: 435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/172.300;
               435/240.200; 435/320.100; 536/023.500; 935/011.000; 935/027.000;
               935/056.000; 935/066.000
NCL     NCLM:  435/252.300
        NCLS:  435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/320.100;
               536/023.500
IC      [5]
        ICM: C12N015-12
        ICS: C12N015-63
EXF     536/27; 536/23.5; 435/69.1; 435/70.1; 435/70.3; 435/71.1; 435/172.3;
        435/240.2; 435/252.3; 435/320.1; 935/8; 935/11; 935/12; 935/24; 935/27;
        935/56; 935/66
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 12 OF 339  USPATFULL
AN      93:102688  USPATFULL
TI      Vitamin K-dependent carboxylase
IN      Stafford, Darrel W., Carrboro, NC, United States
        Wu, Sheue-Mei, Carrboro, NC, United States
PA      The University of North Carolina at Chapel Hill, Chapel Hill, NC, United
        States (U.S. corporation)
PI      US 5268275              19931207
AI      US 1991-756250          19910909 (7)
RLI     Continuation-in-part of Ser. No. US 1991-697427, filed on 8 May 1991,
        now abandoned
DT      Utility
FS      Granted
LN.CNT 1386
INCL    INCLM: 435/691.000
        INCLS: 435/069.600; 435/172.100; 435/172.300; 435/240.200; 435/252.300;
               435/320.100; 536/023.200; 935/010.000; 935/034.000; 935/049.000
NCL     NCLM:  435/069.100
        NCLS:  435/069.600; 435/232.000; 435/252.300; 435/320.100; 435/352.000;
               435/354.000; 435/358.000; 435/366.000; 536/023.200
IC      [5]
        ICM: C12P021-00
        ICS: C12N009-88; C12N001-00; C12N005-00; C12N015-60; C12N015-67;
        C07H021-04
EXF     435/69.1; 435/69.6; 435/110; 435/232; 435/172.1; 435/240.2; 435/320.1;
        435/252.3; 435/240.1; 536/27; 536/23.2; 935/10; 935/34; 935/49
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 13 OF 339  USPATFULL
AN      93:100861  USPATFULL
TI      Polynucleotide sequence for production of glucose oxidase in recombinant
        systems
IN      Rosenberg, Steven, Oakland, CA, United States
PA      Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI      US 5266688              19931130
AI      US 1992-848406          19920306 (7)
RLI     Continuation of Ser. No. US 1989-366377, filed on 19 Jun 1989, now
        patented, Pat. No. US 5094951 which is a continuation of Ser. No. US
        1988-209530, filed on 21 Jun 1988, now abandoned
DT      Utility
FS      Granted
LN.CNT 2005
INCL    INCLM: 536/023.200
        INCLS: 435/320.100
NCL     NCLM:  536/023.200
        NCLS:  435/320.100
IC      [5]
        ICM: C12N015-53
EXF     536/27; 536/23.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 14 OF 339  USPATFULL
AN      93:100856  USPATFULL
TI      Osteogenic proteins
IN      Oppermann, Hermann, Medway, MA, United States
        Ozkaynak, Engin, Milford, MA, United States
        Kuberasampath, Thangavel, Medway, MA, United States
        Rueger, David C., Hopkinton, MA, United States
        Pang, Roy H. L., Medway, MA, United States
PA      Stryker Corporation, Kalamazoo, MI, United States (U.S. corporation)
PI      US 5266683              19931130
AI      US 1992-841646          19920221 (7)
RLI     Continuation-in-part of Ser. No. US 1992-827052, filed on 28 Jan 1992,
        now patented, Pat. No. US 5250302 Ser. No. Ser. No. US 1990-579865,
        filed on 7 Oct 1990, now patented, Pat. No. US 5108753 Ser. No. Ser. No.
        US 1990-621849, filed on 4 Dec 1990, now abandoned Ser. No. Ser. No. US
        1990-621988, filed on 4 Dec 1990, now abandoned Ser. No. Ser. No. US
        1991-810560, filed on 20 Dec 1991, now abandoned Ser. No. Ser. No. US
        1990-569920, filed on 20 Aug 1990, now abandoned Ser. No. Ser. No. US
        1990-600024, filed on 18 Oct 1990, now abandoned Ser. No. Ser. No. US
        1990-599543, filed on 18 Oct 1990, now abandoned Ser. No. Ser. No. US
        1990-616374, filed on 21 Nov 1990, now patented, Pat. No. US 5162114 And
        Ser. No. US 1990-483913, filed on 22 Feb 1990, now patented, Pat. No. US
        5171574 , said Ser. No.    827052 which is a division of Ser. No. US
        1988-179406, filed on 8 Apr 1988, now patented, Pat. No. US 4968590 ,
        said Ser. No.    579865 which is a division of Ser. No.    179406 , said
        Ser. No.    621849 which is a division of Ser. No. US 1988-232630, filed
        on 15 Aug 1988, now abandoned which is a continuation-in-part of Ser.
        No.    179406 , said Ser. No.    621988 which is a division of Ser. No.
        US 1989-315342, filed on 23 Feb 1989, now patented, Pat. No. US 5011691
        which is a continuation-in-part of Ser. No.    232630 , said Ser. No.
        810560 which is a continuation of Ser. No. US 1991-660162, filed on 22
        Feb 1991, now abandoned which is a continuation of Ser. No. US
        1989-422699, filed on 17 Oct 1989, now abandoned which is a
        continuation-in-part of Ser. No.    315342 , said Ser. No.    569920
        which is a continuation-in-part of Ser. No.    422699 And Ser. No.
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        483913 which is a continuation-in-part of Ser. No. US 1989-422613, filed
        on 17 Oct 1989, now patented, Pat. No. US 4975526 which is a
        continuation-in-part of Ser. No.    315342 , said Ser. No.    600024
        which is a continuation-in-part of Ser. No.    569920 , said Ser. No.
        599543 which is a continuation-in-part of Ser. No.    569920 which is a
        continuation-in-part of Ser. No.    569920
DT      Utility
FS      Granted
LN.CNT 4144
INCL    INCLM: 530/326.000
        INCLS: 530/327.000; 530/328.000; 530/350.000; 530/395.000; 530/840.000
NCL     NCLM:  530/326.000
        NCLS:  530/327.000; 530/328.000; 530/350.000; 530/395.000; 530/840.000
IC      [5]
        ICM: A61K037-02
        ICS: C07K005-00; C07K007-00; C07K015-00
EXF     530/326; 530/327; 530/328; 530/395; 530/840; 530/300; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 15 OF 339  USPATFULL
AN      93:100641  USPATFULL
TI      .alpha.-1-antichymotrypsin, analogues and methods of production
IN      Rubin, Harvey, Philadelphia, PA, United States
        Wang, Zhi M., Philadelphia, PA, United States
        Cooperman, Barry S., Penn Valley, PA, United States
        Schecter, Norman, Philadelphia, PA, United States
PA      The Trustees of the University of Pennsylvania, Philadelphia, PA, United
        States (U.S. corporation)
PI      US 5266465              19931130
AI      US 1991-735322          19910724 (7)
RLI     Division of Ser. No. US 1989-370704, filed on 23 Jun 1989, now patented,
        Pat. No. US 5079336
DT      Utility
FS      Granted
LN.CNT 853
INCL    INCLM: 435/069.200
        INCLS: 435/069.100; 435/172.100; 435/172.300; 435/213.000; 530/350.000
NCL     NCLM:  435/069.200
        NCLS:  435/069.100; 435/213.000; 530/350.000
IC      [5]
        ICM: C07K003-00
        ICS: C12P021-02; C12N015-09; A61K045-05
EXF     435/69.1; 435/69.2; 435/172.1; 435/172.3; 435/320.1; 435/213; 530/380;
        530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 16 OF 339  USPATFULL
AN      93:100493  USPATFULL
TI      Insect-specific paralytic neurotoxin genes for use in biological insect
        control: methods and compositions
IN      Tomalski, Michael D., Athens, GA, United States
        Miller, Lois K., Athens, GA, United States
PA      University of Georgia Research Foundation, Inc., Athens, GA, United
        States (U.S. corporation)
PI      US 5266317              19931130
AI      US 1990-593657          19901004 (7)
DT      Utility
FS      Granted
LN.CNT 2085
INCL    INCLM: 424/093.000T
        INCLS: 536/023.500; 435/235.100; 435/069.100; 435/172.300; 435/320.100
NCL     NCLM:  424/093.200
        NCLS:  424/093.600; 435/069.100; 435/235.100; 435/320.100; 536/023.500
IC      [5]
        ICM: C12N007-01
        ICS: C12N015-12
EXF     536/27; 536/93.5; 935/36; 435/69.1; 435/235.1; 435/320.1; 435/172.3;
        424/93; 434/93T
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 17 OF 339  USPATFULL
AN      93:98501  USPATFULL
TI      Polypeptide of a human cripto-related gene, CR-3
IN      Salomon, David S., Germantown, MD, United States
        Persico, Maria G., Naples, Italy
PA      The United States of America as represented by the Department of Health
        and Human Services, Washington, DC, United States (U.S. government)
PI      US 5264557              19931123
AI      US 1991-749001          19910823 (7)
DT      Utility
FS      Granted
LN.CNT 686
INCL    INCLM: 530/399.000
        INCLS: 530/350.000; 530/387.700; 530/387.900; 435/006.000; 435/069.100;
               435/007.230; 536/023.510
NCL     NCLM:  530/399.000
        NCLS:  435/006.000; 435/007.230; 435/069.100; 530/350.000; 530/387.700;
               530/387.900; 536/023.510
IC      [5]
        ICM: C07K003-00
        ICS: A61K037-24; C12P021-06; C07H015-12
EXF     435/69.1; 435/6; 435/7.23; 530/350; 530/387; 530/388; 530/399; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 18 OF 339  USPATFULL
AN      93:98498  USPATFULL
TI      Platelet cell adhesion molecule and variants thereof
IN      Newman, Peter J., Shorewood, WI, United States
PA      The Blood Center of Southeastern Wisconsin, Inc., Milwaukee, WI, United
        States (U.S. corporation)
PI      US 5264554              19931123
AI      US 1990-466140          19900119 (7)
DT      Utility
FS      Granted
LN.CNT 772
INCL    INCLM: 530/387.100
        INCLS: 530/395.000; 530/350.000; 530/324.000; 435/069.100; 424/085.800
NCL     NCLM:  530/387.100
        NCLS:  435/069.100; 530/324.000; 530/350.000; 530/387.900; 530/395.000;
               536/023.500
IC      [5]
        ICM: C07K013-00
        ICS: C07K009-00; C07K015-14; A61K039-00
EXF     530/387; 530/388; 530/380; 530/395; 530/330; 530/329; 530/328; 530/327;
        530/326; 530/325; 530/324; 530/350; 530/387.1; 514/8; 514/12; 435/69.1;
        424/85.8
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 19 OF 339  USPATFULL
AN      93:98494  USPATFULL
TI      Human anti-inflammatory phospholipase inhibitor protein
IN      Johnson, Lorin K., Pleasanton, CA, United States
        Longenecker, John P., Mt. View, CA, United States
PA      Scios Nova Inc., Mountain View, CA, United States (U.S. corporation)
PI      US 5264550              19931123
AI      US 1992-871577          19920420 (7)
RLI     Continuation of Ser. No. US 1990-538692, filed on 14 Jun 1990, now
        abandoned which is a continuation of Ser. No. US 1986-883598, filed on 9
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       Jul 1986, now abandoned which is a continuation-in-part of Ser. No. US
       1985-723046, filed on 15 Apr 1985, now abandoned
DT     Utility
FS     Granted
LN.CNT 1582
INCL   INCLM: 530/350.000
       INCLS: 530/395.000; 530/851.000; 435/692.000
NCL    NCLM:  530/350.000
       NCLS:  435/069.200; 530/395.000; 530/851.000
IC     [5]
       ICM: C07K013-00
EXF    530/350; 530/395; 530/851; 435/69.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 20 OF 339  USPATFULL
AN     93:96243  USPATFULL
TI     cDNA probe differentiating normal and cancer tissues
IN     Sager, Ruth, Brookline, MA, United States
       Lee, Sam W., Boston, MA, United States
       Tomasetto, Catherine, Boston, MA, United States
PA     Dana-Farber Cancer Institute, Inc., Boston, MA, United States (U.S.
       corporation)
PI     US 5262528              19931116
AI     US 1991-662198          19910228 (7)
DT     Utility
FS     Granted
LN.CNT 306
INCL   INCLM: 536/024.310
       INCLS: 435/172.300; 435/252.300
NCL    NCLM:  536/024.310
       NCLS:  435/252.300
IC     [5]
       ICM: C12N015-11
       ICS: C12N001-21
EXF    536/27; 536/24.31; 530/300; 530/828; 530/387.7; 435/172.3; 435/240.2;
       435/252.3
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 21 OF 339  USPATFULL
AN     93:96237  USPATFULL
TI     Receptor for oncostatin M and leukemia inhibitory factor
IN     Gearing, David P., Seattle, WA, United States
PA     Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI     US 5262522              19931116
AI     US 1991-797556          19911122 (7)
DT     Utility
FS     Granted
LN.CNT 2133
INCL   INCLM: 530/350.000
       INCLS: 435/069.700; 435/252.300; 435/370.100
NCL    NCLM:  530/350.000
       NCLS:  435/069.700; 435/252.300; 435/320.100
IC     [5]
       ICM: C07K013-00
       ICS: C12N015-62
EXF    435/69.1; 435/69.7; 530/350; 530/387; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 22 OF 339  USPATFULL
AN     93:96042  USPATFULL
TI     Host transformed with yeast gene and ubiquitin/polypeptide fusions
IN     Liu, Chung-Cheng, Foster City, CA, United States
       Miller, Harvey I., Pleasant Hill, CA, United States
PA     Genentech, Inc., South San Francisco, CA, United States (U.S.
       corporation)
PI     US 5262322              19931116
AI     US 1991-694522          19910430 (7)
RLI    Division of Ser. No. US 1988-284281, filed on 14 Dec 1988, now patented,
       Pat. No. US 5108919 which is a continuation-in-part of Ser. No. US
       1988-210909, filed on 24 Jun 1988, now patented, Pat. No. US 5156968
DT     Utility
FS     Granted
LN.CNT 2176
INCL   INCLM: 435/252.330
       INCLS: 435/069.700; 435/172.300; 435/195.000; 435/224.000; 435/252.300;
              435/320.100; 536/023.200; 536/023.400
NCL    NCLM:  435/252.330
       NCLS:  435/069.700; 435/195.000; 435/224.000; 435/252.300; 435/320.100;
              536/023.200; 536/023.400
IC     [5]
       ICM: C12N001-21
EXF    435/252.33; 435/252.3; 435/69.7; 435/172.3; 435/195; 435/224; 435/320.1;
       536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 23 OF 339  USPATFULL
AN     93:96039  USPATFULL
TI     Method for obtaining bone marrow free of tumor cells using transforming
       growth factor .beta.3
IN     Iwata, Kenneth K., Westbury, NY, United States
       Foulkes, J. Gordon, Huntington, NY, United States
       Dijke, Peter T., Port Washington, NY, United States
       Haley, John D., Great Neck, NY, United States
PA     Oncogene Science, Inc., Uniondale, NY, United States (U.S. corporation)
PI     US 5262319              19931116
AI     US 1990-543341          19900625 (7)
RLI    Continuation-in-part of Ser. No. US 1989-353410, filed on 17 May 1989,
       now abandoned which is a continuation-in-part of Ser. No. US
       1988-183824, filed on 20 Apr 1988, now abandoned which is a
       continuation-in-part of Ser. No. US 1987-111022, filed on 20 Oct 1987
       which is a continuation-in-part of Ser. No. US 1986-922121, filed on 20
       Oct 1986, now abandoned which is a continuation-in-part of Ser. No. US
       1986-847931, filed on 7 Apr 1986, now abandoned which is a
       continuation-in-part of Ser. No. US 1985-725003, filed on 19 Apr 1985,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 1446
INCL   INCLM: 435/240.200
       INCLS: 435/240.250; 530/399.000
NCL    NCLM:  435/378.000
       NCLS:  530/399.000
IC     [5]
       ICM: C12N005-08
       ICS: C07K015-14
EXF    435/240.2; 435/240.21; 435/240.25; 514/2; 514/8; 514/25; 530/395;
       530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 24 OF 339  USPATFULL
AN     93:95898  USPATFULL
TI     Recombinant viruses encoding the human melanoma-associated antigen
IN     Brown, Joseph P., Seattle, WA, United States
       Estin, Charles D., Bainbridge Island, WA, United States
       Plowman, Gregory D., Seattle, WA, United States
       Rose, Timothy M., Seattle, WA, United States
       Hellstrom, Karl E., Seattle, WA, United States
       Hellstrom, Ingegerd, Seattle, WA, United States
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       Purchio, Anthony F., Seattle, WA, United States
       Hu, Shiu-Lok, Redmond, WA, United States
       Pennathur, Sridhar, Seattle, WA, United States
PA     Oncogen, Seattle, WA, United States (U.S. corporation)
PI     US 5262177              19931116
AI     US 1987-7230            19870127 (7)
RLI    Continuation-in-part of Ser. No. US 1986-827313, filed on 7 Feb 1986,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 1993
INCL   INCLM: 424/089.000
       INCLS: 435/069.300; 435/172.300; 435/235.100; 435/320.100; 435/252.300;
              435/252.330; 435/240.200; 536/023.500; 530/350.000; 835/009.000;
              835/032.000; 835/041.000; 835/057.000; 835/065.000; 835/070.000;
              835/073.000
NCL    NCLM:  435/235.100
       NCLS:  424/185.100; 424/199.100; 424/232.100; 435/069.300; 435/252.300;
              435/252.330; 435/320.100; 435/362.000; 530/350.000; 536/023.500
IC     [5]
       ICM: A61K039-12
       ICS: C12P021-02; C12P019-34; C12N015-00; C12N007-00; C12N005-00;
       C12N001-21; C12N001-16
EXF    435/68; 435/70; 435/172.1; 435/172.3; 435/235; 435/236; 435/320;
       435/69.3; 435/91; 435/235.1; 435/320.1; 435/252.33; 435/255; 435/256;
       435/240.2; 424/89; 536/27; 530/350; 835/9; 835/32; 835/41; 835/57;
       835/65; 835/70; 835/73
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 25 OF 339  USPATFULL
AN     93:93905  USPATFULL
TI     Antigenic epitopes present on membrane-bound but not secreted IgE
IN     Chang, Tse-wen, Houston, TX, United States
PA     Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI     US 5260416              19931109
AI     US 1990-468766          19900123 (7)
RLI    Continuation-in-part of Ser. No. US 1989-369625, filed on 21 Jun 1989,
       now abandoned which is a continuation-in-part of Ser. No. US
       1988-272243, filed on 16 Nov 1988, now patented, Pat. No. US 5091313
       which is a continuation-in-part of Ser. No. US 1988-229178, filed on 5
       Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US
       1988-226421, filed on 29 Jul 1988 which is a continuation-in-part of
       Ser. No. US 1987-140036, filed on 31 Dec 1987, now abandoned
DT     Utility
FS     Granted
LN.CNT 859
INCL   INCLM: 530/327.000
       INCLS: 530/387.200; 530/387.300; 530/388.730; 530/862.000; 530/868.000;
              424/085.800
NCL    NCLM:  530/327.000
       NCLS:  424/131.100; 424/139.100; 424/140.100; 424/153.100; 424/805.000;
              424/810.000; 530/387.200; 530/387.300; 530/388.730; 530/862.000;
              530/868.000
IC     [5]
       ICM: C07K007-08
       ICS: C07K017-02
EXF    530/327; 530/388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 26 OF 339  USPATFULL
AN     93:93760  USPATFULL
TI     Odorant-binding protein from rat
IN     Snyder, Solomon H., Baltimore, MD, United States
       Pevsner, Jonathan, Baltimore, MD, United States
       Reed, Randall, Baltimore, MD, United States
PA     The Johns Hopkins University, Baltimore, MD, United States (U.S.
       corporation)
PI     US 5260270              19931109
AI     US 1991-730074          19910715 (7)
RLI    Division of Ser. No. US 1990-628429, filed on 17 Dec 1990 which is a
       division of Ser. No. US 1990-492792, filed on 13 Mar 1990 which is a
       division of Ser. No. US 1988-175180, filed on 30 Mar 1988, now patented,
       Pat. No. US 5030722, issued on 9 Jul 1991
DT     Utility
FS     Granted
LN.CNT 839
INCL   INCLM: 514/002.000
       INCLS: 514/012.000; 530/350.000; 935/107.000
NCL    NCLM:  514/002.000
       NCLS:  514/012.000; 530/350.000
IC     [5]
       ICM: A61K037-02
       ICS: C07K013-00
EXF    436/503; 436/501; 512/2; 512/4; 514/2; 514/12; 530/350; 935/107
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 27 OF 339  USPATFULL
AN     93:93713  USPATFULL
TI     Methods for detection of human gamma, .gamma. T cell receptor
IN     Brenner, Michael B., Ashland, MA, United States
       Strominger, Jack L., Lexington, MA, United States
       Seidman, John G., Milton, MA, United States
       Ip, Stephen H., Framingham, MA, United States
       Krangel, Michael S., Newtonville, MA, United States
PA     President & Fellows of Harvard College, Boston, MA, United States (U.S.
       corporation)
       Dana Farber Cancer Institute & T Cell Diagnostics, Inc., Boston, MA,
       United States (U.S. corporation)
PI     US 5260223              19931109
AI     US 1988-187698          19880429 (7)
RLI    Continuation-in-part of Ser. No. US 1987-115256, filed on 29 Oct 1987,
       now patented, Pat. No. US 5024940, issued on 18 Jun 1991 which is a
       continuation-in-part of Ser. No. US 1987-16252, filed on 19 Feb 1987
       which is a continuation-in-part of Ser. No. US 1986-882100, filed on 3
       Jul 1986, now abandoned
DT     Utility
FS     Granted
LN.CNT 1745
INCL   INCLM: 436/501.000
       INCLS: 435/007.100; 435/007.240; 435/172.200; 435/240.270; 436/506.000;
              436/518.000; 436/548.000; 436/064.000; 530/387.900; 530/388.220;
              530/388.750; 530/350.000; 536/023.500
NCL    NCLM:  436/501.000
       NCLS:  435/007.100; 435/007.240; 436/064.000; 436/506.000; 436/518.000;
              436/548.000; 530/350.000; 530/387.900; 530/388.220; 530/388.750;
              536/023.500
IC     [5]
       ICM: G01N033-566
EXF    435/7; 435/172.2; 435/240.27; 435/69.6; 435/7.1; 435/7.23; 436/501;
       436/506; 436/518; 436/548; 436/811; 436/813; 436/64; 530/350; 530/387;
       530/395; 530/828; 530/829; 935/110
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 28 OF 339  USPATFULL
AN     93:93700  USPATFULL
TI     Nucleic acids encoding dystrophin-associated proteins
IN     Campbell, Kevin P., Iowa City, IA, United States
       Ibraghimov-Beskrovnaya, Oxana, Iowa City, IA, United States
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       Ervasti, James M., Iowa City, IA, United States
       Leveille, Cynthia J., Iowa City, IA, United States
PA     University of Iowa Research Foundation, Oakdale, IA, United States (U.S.
       corporation)
PI     US 5260209              19931109
AI     US 1992-841654          19920220 (7)
RLI    Continuation-in-part of Ser. No. US 1990-527583, filed on 23 May 1990,
       now patented, Pat. No. US 5187063
DT     Utility
FS     Granted
LN.CNT 1820
INCL   INCLM: 435/240.200
       INCLS: 435/069.100; 435/070.300; 435/071.100; 435/071.200; 435/172.300;
              435/252.300; 435/320.100; 536/023.500; 935/011.000; 935/027.000;
              935/056.000; 530/350.000
NCL    NCLM:  435/325.000
       NCLS:  435/069.100; 435/070.300; 435/071.100; 435/071.200; 435/252.300;
              435/320.100; 530/350.000; 536/023.500
IC     [5]
       ICM: C12N015-12
       ICS: C12N015-74; C12N015-79
EXF    435/69.1; 435/70.3; 435/71.1; 435/71.2; 435/172.3; 435/240.2; 435/252.3;
       435/320.1; 536/27; 536/23.5; 530/380; 935/11; 935/27; 935/56
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 29 OF 339  USPATFULL
AN     93:93691  USPATFULL
TI     Isolated DNA encoding an insulin receptor substrate
IN     Kahn, C. Ronald, West Newton, MA, United States
       White, Morris F., West Roxbury, MA, United States
       Rothenberg, Paul L., Narberth, PA, United States
PA     Joslin Diabetes Center, Inc., Boston, MA, United States (U.S.
       corporation)
PI     US 5260200              19931109
AI     US 1992-962023          19921015 (7)
RLI    Continuation of Ser. No. US 1991-643982, filed on 18 Jan 1991, now
       abandoned
DT     Utility
FS     Granted
LN.CNT 2797
INCL   INCLM: 435/068.100
       INCLS: 435/252.300; 435/320.100; 530/350.000; 536/023.500
NCL    NCLM:  435/069.100
       NCLS:  435/252.300; 435/320.100; 530/350.000; 536/023.500
IC     [5]
       ICM: C07K013-00
       ICS: C12N015-12; C12N015-63
EXF    435/69.1; 435/252.3; 435/330.1; 530/350; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 30 OF 339  USPATFULL
AN     93:91549  USPATFULL
TI     Fluorophore-assisted cloning analysis
IN     Starr, Christopher M., Sonoma, CA, United States
       Klock, John C., Mill Valley, CA, United States
PA     Glyko, Inc., Novato, CA, United States (U.S. corporation)
PI     US 5258295              19931102
AI     US 1992-840739          19920225 (7)
DT     Utility
FS     Granted
LN.CNT 796
INCL   INCLM: 435/172.300
       INCLS: 435/007.400; 536/001.110
NCL    NCLM:  435/006.000
       NCLS:  435/007.400; 536/001.110
IC     [5]
       ICM: C12N015-10
EXF    435/172.3; 935/9; 935/1; 935/6; 935/15; 935/19; 935/79; 935/80
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 31 OF 339  USPATFULL
AN     93:91542  USPATFULL
TI     Vector containing DNA encoding mature human protein S
IN     Wydro, Robert, Framingham, MA, United States
       Cohen, Edward, Natick, MA, United States
       Dackowski, William, Hopkinton, MA, United States
       Stenflo, Johan, Malmo, Sweden
       Lundwall, Ake, Lund, Sweden
       Dahlback, Bjorn, Malmo, Sweden
PA     Genzyme Corporation, Cambridge, MA, United States (U.S. corporation)
PI     US 5258288              19931102
AI     US 1986-890401          19860725 (6)
DT     Utility
FS     Granted
LN.CNT 529
INCL   INCLM: 435/069.600
       INCLS: 435/069.100; 435/172.300; 435/320.100; 435/235.100; 435/240.200;
              536/023.500; 530/350.000; 935/019.000; 935/032.000; 935/041.000;
              935/057.000; 935/062.000; 935/070.000
NCL    NCLM:  435/069.600
       NCLS:  435/069.100; 435/235.100; 435/320.100; 435/354.000; 530/350.000;
              536/023.500
IC     [5]
       ICM: C12P021-02
       ICS: C12P019-34; C12N015-00; C12N007-00; C12N005-00; C07K003-00;
       C07H015-12
EXF    435/68; 435/172.3; 435/320; 435/240; 435/69.1; 435/91; 435/235;
       435/240.1; 435/320.1; 435/252.3; 530/350; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 32 OF 339  USPATFULL
AN     93:91541  USPATFULL
TI     DNA encoding and methods of production of insulin-like growth factor
       binding protein BP53
IN     Baxter, Robert C., Plebe, Australia
       Wood, William I., San Mateo, CA, United States
PA     Genentech, Inc., South San Francisco, CA, United States (U.S.
       corporation)
       Central Sydney Area Health Service, Camperdown, Australia (non-U.S.
       corporation)
PI     US 5258287              19931102
AI     US 1988-171623          19880322 (7)
DT     Utility
FS     Granted
LN.CNT 1665
INCL   INCLM: 435/069.100
       INCLS: 536/023.500; 435/006.000; 435/069.800; 435/240.100; 435/240.200;
              435/252.300; 435/254.110; 435/254.200; 435/320.100
NCL    NCLM:  435/069.100
       NCLS:  435/006.000; 435/069.800; 435/252.300; 435/254.110; 435/254.200;
              435/320.100; 435/365.000; 435/369.000; 536/023.500
IC     [5]
       ICM: C12N005-10
       ICS: C12N001-15; C12N001-21; C12N015-12
EXF    435/69.1; 435/6; 435/172.3; 435/69.8; 435/320.1; 435/254; 435/255;
       435/256; 435/240.2; 435/240.1; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L6    ANSWER 33 OF 339  USPATFULL
AN      93:89649  USPATFULL
TI      Compositions of soluble complement receptor 1 (CR1) and a thrombolytic
        agent, and the methods of use thereof
IN      Fearon, Douglas T., Baltimore, MD, United States
        Klickstein, Lloyd B., Brookline, MA, United States
        Wong, Winnie W., Newton, MA, United States
        Carson, Gerald R., Wellesley, MA, United States
        Concino, Michael F., Newton, MA, United States
        Ip, Stephen H., Sudbury, MA, United States
        Makrides, Savvas, C., Bedford, MA, United States
        Marsh, Jr., Henry C., Reading, MA, United States
PA      The Johns Hopkins University, Baltimore, MD, United States (U.S.
        corporation)
        Brigham and Women's Hospital, Boston, MA, United States (U.S.
        corporation)
        T Cell Sciences, Inc., Cambridge, MA, United States (U.S. corporation)
PI      US 5256642              19931026
AI      US 1990-588128          19900924 (7)
RLI     Continuation-in-part of Ser. No. US 1989-412745, filed on 26 Sep 1989,
        now abandoned which is a continuation-in-part of Ser. No. US
        1989-332865, filed on 3 Apr 1989, now abandoned which is a
        continuation-in-part of Ser. No. US 1988-176532, filed on 1 Apr 1988,
        now abandoned
DT      Utility
FS      Granted
LN.CNT 4529
INCL    INCLM: 514/008.000
        INCLS: 514/002.000; 424/094.630; 424/094.640; 435/215.000; 435/216.000;
               530/350.000
NCL     NCLM:  514/008.000
        NCLS:  424/094.630; 424/094.640; 435/215.000; 435/216.000; 514/002.000;
               530/350.000
IC      [5]
        ICM: A61K037-02
        ICS: A61K037-547; C12N009-72; C07K013-00
EXF     424/94.63; 424/94.64; 514/2; 514/8; 435/215; 435/216; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 34 OF 339  USPATFULL
AN      93:89568  USPATFULL
TI      Primitive cell colony stimulating factors and lymphohematopoietic
        progenitor cells
IN      Lawman, Michael J. P., Gainsville, FL, United States
        Ohmann, Helle B., Saskatchewan, Canada
        Attah-Poku, Samuel K., Saskatchewan, Canada
        Heise-Qualtiere, Janette, Saskatchewan, Canada
PA      University of Saskatchewan, Saskatoon, Canada (non-U.S. corporation)
PI      US 5256560              19931026
AI      US 1991-677617          19910327 (7)
RLI     Continuation of Ser. No. US 1988-255088, filed on 7 Oct 1988, now
        abandoned
DT      Utility
FS      Granted
LN.CNT 1557
INCL    INCLM: 435/240.200
        INCLS: 435/240.210; 435/240.250
NCL     NCLM:  435/325.000
        NCLS:  435/372.000
IC      [5]
        ICM: C12N005-00
        ICS: C12N005-02
EXF     435/240.1; 435/240.2; 435/240.25; 435/240.3; 435/240.21; 435/240.25;
        514/2; 424/93U; 424/577
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 35 OF 339  USPATFULL
AN      93:89566  USPATFULL
TI      Gene encoding plant asparagine synthetase
IN      Coruzzi, Gloria M., New York, NY, United States
        Tsai, Fong-Ying, New York, NY, United States
PA      The Trustees of Rockefeller University, New York, NY, United States
        (U.S. corporation)
PI      US 5256558              19931026
AI      US 1990-514816          19900426 (7)
RLI     Continuation-in-part of Ser. No. US 1989-347302, filed on 3 May 1989,
        now abandoned
DT      Utility
FS      Granted
LN.CNT 1994
INCL    INCLM: 435/240.100
        INCLS: 435/252.300; 435/320.100; 435/172.300; 435/252.330; 536/023.200;
               536/024.100
NCL     NCLM:  435/252.330
        NCLS:  435/252.300; 435/320.100; 536/023.200; 536/024.100
IC      [5]
        ICM: C12N005-10
        ICS: C12N001-19; C12N001-21; C12N015-52
EXF     435/91; 435/172.3; 435/240.1; 435/252.3; 435/252.33; 435/254; 435/255;
        435/183; 435/320.1; 536/27; 935/33; 935/34; 935/35
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 36 OF 339  USPATFULL
AN      93:87584  USPATFULL
TI      Heterologous dominant conditional lethal gene which is a phosphonate
        monoester hydrolase and use thereof in plants
IN      Dotson, Stanton B., Fenton, MO, United States
        Kishore, Ganesh M., Chesterfield, MO, United States
PA      Monsanto Company, St. Louis, MO, United States (U.S. corporation)
PI      US 5254801              19931019
AI      US 1990-621670          19901203 (7)
DT      Utility
FS      Granted
LN.CNT 2021
INCL    INCLM: 800/205.000
        INCLS: 435/240.400; 435/172.300; 435/320.100; 435/069.100; 935/064.000;
               935/067.000; 800/DIG.015
NCL     NCLM:  800/287.000
        NCLS:  435/069.100; 435/320.100; 435/419.000; 536/023.200; 800/298.000;
               800/303.000
IC      [5]
        ICM: A01H004-00
        ICS: C12N005-14; C12N015-82
EXF     800/205; 800/DIG.15; 435/320.1; 435/172.3; 435/240.4; 435/69.1; 536/27;
        935/64; 935/67
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 37 OF 339  USPATFULL
AN      93:87456  USPATFULL
TI      Extracellular segments of human e immunoglobulin anchoring peptides and
        antibodies specific therefor
IN      Chang, Tse W., Houston, TX, United States
PA      Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI      US 5254671              19931019
AI      US 1992-973321          19921029 (7)
RLI     Continuation-in-part of Ser. No. US 1990-515604, filed on 27 Apr 1990,
        now abandoned
DT      Utility
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FS      Granted
LN.CNT 1331
INCL    INCLM: 530/324.000
        INCLS: 530/350.000; 530/386.000; 536/023.530
NCL     NCLM:  530/324.000
        NCLS:  530/350.000; 530/386.000; 536/023.530
IC      [5]
        ICM: C07K007-10
        ICS: C12N015-13
EXF     536/23.23; 536/23.53; 530/324; 530/350; 530/386
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 38 OF 339  USPATFULL
AN      93:87246  USPATFULL
TI      Nucleotide and amino acid sequences of protein MTP40 of M. tuberculosis
        and synthetic peptides derived therefrom
IN      Patarroyo, Manuel E., Calle 135 No.15-40, Bogota, Colombia.
PI      US 5254459              19931019
AI      US 1992-940468          19920904 (7)
RLI     Division of Ser. No. US 1990-572171, filed on 23 Aug 1990, now patented,
        Pat. No. US 5171839
DT      Utility
FS      Granted
LN.CNT 535
INCL    INCLM: 435/006.000
        INCLS: 435/732.000; 435/810.000; 435/863.000; 530/350.000; 530/326.000;
               536/023.700; 536/024.320; 436/063.000; 436/808.000; 424/092.000
NCL     NCLM:  435/006.000
        NCLS:  424/190.100; 424/248.100; 435/007.320; 435/810.000; 435/863.000;
               436/063.000; 436/808.000; 530/326.000; 530/350.000; 536/023.700;
               536/024.320
IC      [5]
        ICM: C12Q001-68
        ICS: G01N033-569
EXF     530/350; 435/6; 435/7.32; 435/863; 435/810; 424/92; 436/63; 436/808
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 39 OF 339  USPATFULL
AN      93:85275  USPATFULL
TI      .alpha.-1-antichymotrypsin, analogues and methods of production
IN      Rubin, Harvey, Philadelphia, PA, United States
        Wang, Zhi M., Philadelphia, PA, United States
PA      The Trustees of the University of Pennsylvania, Philadelphia, PA, United
        States (U.S. corporation)
PI      US 5252725              19931012
AI      US 1991-735335          19910724 (7)
RLI     Division of Ser. No. US 1989-370704, filed on 23 Jun 1989, now patented,
        Pat. No. US 5079336
DT      Utility
FS      Granted
LN.CNT 836
INCL    INCLM: 536/023.500
        INCLS: 435/069.200; 435/172.100; 435/172.300; 435/213.000; 435/320.100
NCL     NCLM:  536/023.500
        NCLS:  435/069.200; 435/213.000; 435/320.100
IC      [5]
        ICM: C07H021-00
        ICS: C07K003-00; C12N015-09; A61K045-05
EXF     435/69.1; 435/69.2; 435/172.1; 435/172.3; 435/213; 435/320.1; 530/380;
        536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 40 OF 339  USPATFULL
AN      93:85267  USPATFULL
TI      Marek's disease herpesvirus DNA segments encoding glycoproteins, gD, gI
        and gE
IN      Velicer, Leland F., East Lansing, MI, United States
        Brunovskis, Peter, East Lansing, MI, United States
        Coussens, Paul M., DeWitt, MI, United States
PA      Board of Trustees operating Michigan State University, East Lansing, MI,
        United States (U.S. corporation)
PI      US 5252717              19931012
AI      US 1992-848697          19920309 (7)
RLI     Division of Ser. No. US 1990-572711, filed on 24 Aug 1990, now patented,
        Pat. No. US 5138033
DT      Utility
FS      Granted
LN.CNT 941
INCL    INCLM: 530/395.000
NCL     NCLM:  530/395.000
IC      [5]
        ICM: C07K013-00
EXF     530/395; 424/89
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 41 OF 339  USPATFULL
AN      93:85266  USPATFULL
TI      Marek's disease herpesvirus DNA segments encoding glycoproteins, gD, gI
        and gE
IN      Velicer, Leland F., East Lansing, MI, United States
        Brunovskis, Peter, East Lansing, MI, United States
        Coussens, Paul M., DeWitt, MI, United States
PA      Board of Trustees operating Michigan State University, East Lansing, MI,
        United States (U.S. corporation)
PI      US 5252716              19931012
AI      US 1992-845957          19920304 (7)
RLI     Division of Ser. No. US 1990-572711, filed on 24 Aug 1990, now patented,
        Pat. No. US 5138030
DT      Utility
FS      Granted
LN.CNT 944
INCL    INCLM: 530/395.000
NCL     NCLM:  530/395.000
IC      [5]
        ICM: C07K013-00
EXF     530/395; 424/89
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 42 OF 339  USPATFULL
AN      93:85018  USPATFULL
TI      Method of making antibodies to antigenic epitopes of IGE
        present on B cells but not basophil cell surface or secreted, soluble
        IGE
IN      Chang, Tse W., Houston, TX, United States
PA      Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI      US 5252467              19931012
AI      US 1992-817916          19920106 (7)
RLI     Division of Ser. No. US 1988-272243, filed on 16 Nov 1988, now patented,
        Pat. No. US 5091313 which is a continuation-in-part of Ser. No. US
        1988-229178, filed on 5 Aug 1988, now abandoned which is a
        continuation-in-part of Ser. No. US 1988-226421, filed on 29 Jul 1988
        which is a continuation-in-part of Ser. No. US 1987-140036, filed on 31
        Dec 1987, now abandoned
DT      Utility
FS      Granted
LN.CNT 693
INCL    INCLM: 435/070.210
        INCLS: 435/172.200; 435/240.270; 530/388.250; 530/389.300; 424/085.800;
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                514/014.000
NCL      NCLM:  435/070.210
         NCLS:  424/153.100; 424/805.000; 424/810.000; 435/452.000; 514/014.000;
                530/388.250; 530/388.730; 530/389.300; 530/862.000; 530/868.000
IC       [5]
         ICM: C12P021-08
         ICS: C12N015-02; C12N005-12; C07K015-28
EXF      530/388.25; 530/389.3; 435/240.27; 435/172.2; 435/70.21; 514/14;
         424/85.8
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 43 OF 339  USPATFULL
AN       93:80738  USPATFULL
TI       Methods for inhibiting neoplastic cell proliferation using platelet
         factor 4
IN       Twardzik, Daniel R., Bainbridge Island, WA, United States
         Todaro, George J., Seattle, WA, United States
PA       Oncogen, Seattle, WA, United States (U.S. corporation)
PI       US 5248666              19930928
AI       US 1992-877341          19920429 (7)
RLI      Continuation of Ser. No. US 1988-159935, filed on 24 Feb 1988, now
         abandoned which is a continuation-in-part of Ser. No. US 1987-115139,
         filed on 30 Oct 1987, now abandoned which is a continuation-in-part of
         Ser. No. US 1987-20609, filed on 2 Mar 1987, now abandoned which is a
         continuation-in-part of Ser. No. US 1986-912407, filed on 26 Sep 1986,
         now patented, Pat. No. US 4737580 which is a division of Ser. No. US
         1985-712302, filed on 15 Mar 1985, now patented, Pat. No. US 4645828,
         issued on 24 Feb 1987 which is a continuation-in-part of Ser. No. US
         1984-592969, filed on 23 Mar 1984, now patented, Pat. No. US 4590003,
         issued on 20 May 1986
DT       Utility
FS       Granted
LN.CNT 1399
INCL     INCLM: 514/012.000
         INCLS: 514/002.000; 424/085.100; 530/324.000
NCL      NCLM:  514/012.000
         NCLS:  424/085.100; 514/002.000; 530/324.000
IC       [5]
         ICM: A61K037-02
EXF      514/2; 514/12; 530/324; 424/85.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 44 OF 339  USPATFULL
AN       93:80681  USPATFULL
TI       Monoclonal antibodies and hybridomas specific for green-oat
         phytochrome
IN       Cordonnier, Marie-Michele, Durham, NC, United States
         Pratt, Lee, Athens, GA, United States
         Stewart, Sandy, Durham, NC, United States
         Montoya, Alice, Durham, NC, United States
PA       Ciba-Geigy Corporation, Hawthorne, NY, United States (U.S. corporation)
PI       US 5248607              19930928
AI       US 1988-263618          19881027 (7)
DT       Utility
FS       Granted
LN.CNT 754
INCL     INCLM: 435/240.270
         INCLS: 530/388.100; 530/391.100; 530/370.000; 435/172.200; 435/070.210
NCL      NCLM:  435/341.000
         NCLS:  435/070.210; 530/370.000; 530/388.100; 530/391.100
IC       [5]
         ICM: C12N005-12
         ICS: C12P021-08; C07K015-28
EXF      530/387; 530/370; 530/388.1; 530/391.1; 435/240.27; 435/172.2; 435/70.21
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 45 OF 339  USPATFULL
AN       93:80677  USPATFULL
TI       Superoxide dismutase
IN       Marklund, Stefan, Ume.ang., Sweden
         Edlund, Thomas, Ume.ang., Sweden
PA       Symbicom Aktiebolag, Umea, Sweden (non-U.S. corporation)
PI       US 5248603              19930928
AI       US 1992-897624          19920612 (7)
RLI      Continuation of Ser. No. US 1990-576114, filed on 27 Aug 1990, now
         patented, Pat. No. US 5130245 which is a continuation of Ser. No. US
         1986-902596, filed on 2 Sep 1986, now abandoned
PRAI     SE 1985-4027        19850903
DT       Utility
FS       Granted
LN.CNT 2242
INCL     INCLM: 435/189.000
         INCLS: 435/240.200; 435/320.100; 536/023.200
NCL      NCLM:  435/189.000
         NCLS:  435/320.100; 435/358.000; 536/023.200
IC       [5]
         ICM: C12N009-02
         ICS: C12N015-53
EXF      435/189; 435/320.1; 435/240.2; 536/27; 536/23.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 46 OF 339  USPATFULL
AN       93:78699  USPATFULL
TI       Bacillus thuringiensis isolate active against lepidopteran pests, and
         genes encoding novel lepidopteran-active toxins
IN       Payne, Jewel, San Diego, CA, United States
         Sick, August J., San Diego, CA, United States
PA       Mycogen Corporation, San Diego, CA, United States (U.S. corporation)
PI       US 5246852              19930921
AI       US 1991-714413          19910612 (7)
RLI      Division of Ser. No. US 1989-371955, filed on 27 Jun 1989, now patented,
         Pat. No. US 5126133
DT       Utility
FS       Granted
LN.CNT 836
INCL     INCLM: 435/252.310
         INCLS: 435/069.100; 435/172.300; 435/252.300; 435/252.330; 435/252.340;
                435/252.350; 435/320.100; 424/093.000A; 536/023.710
NCL      NCLM:  435/252.310
         NCLS:  424/093.200; 424/093.210; 435/069.100; 435/252.300; 435/252.330;
                435/252.340; 435/252.350; 435/320.100; 536/023.710
IC       [5]
         ICM: C12N001-21
         ICS: C12N015-32; C12N015-70; A01N063-00
EXF      435/69.1; 435/71.1; 435/91; 435/172.1; 435/172.3; 435/252.1; 435/252.3;
         435/252.31; 435/252.34; 435/252.35; 435/320.1; 424/93; 935/6; 935/9;
         935/22; 935/59; 935/60; 935/61; 935/64; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6    ANSWER 47 OF 339  USPATFULL
AN       93:78691  USPATFULL
TI       Virulence associated proteins in Borrelia burgdorferi (BB)
IN       Norris, Steven J., Houston, TX, United States
         Barbour, Alan G., San Antonio, TX, United States
PA       Board of Regents, The University of Texas System, Austin, TX, United
         States (U.S. corporation)
PI       US 5246844              19930921
AI       US 1991-781355          19911022 (7)
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DT      Utility
FS      Granted
LN.CNT 1705
INCL    INCLM: 435/172.300
        INCLS: 435/252.300; 435/252.330; 435/320.100; 536/023.700; 536/024.320;
               536/024.330
NCL     NCLM:  435/480.000
        NCLS:  435/252.300; 435/252.330; 435/320.100; 435/476.000; 435/488.000;
               536/023.700; 536/024.320; 536/024.330
IC      [5]
        ICM: C12N015-00
        ICS: C12N015-03; C12N015-31
EXF     536/27; 435/6; 424/92
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 48 OF 339  USPATFULL
AN      93:76631  USPATFULL
TI      Acute phase protein modulating endotoxic activity of
        lipopolysaccharides, assay methods and polypeptides
IN      Ulevitch, Richard, 1127 La Cuchara, Del Mar, CA, United States  92014
        Tobias, Peter, 564 Arden Dr., Encinitas, CA, United States  92024
PI      US 5245013              19930914
AI      US 1989-367454          19890616 (7)
RLI     Continuation-in-part of Ser. No. US 1986-6710, filed on 30 Dec 1986, now
        abandoned which is a continuation-in-part of Ser. No. US 1985-728833,
        filed on 30 Apr 1985, now abandoned
DT      Utility
FS      Granted
LN.CNT 2243
INCL    INCLM: 530/380.000
        INCLS: 530/350.000; 530/395.000
NCL     NCLM:  530/380.000
        NCLS:  530/350.000; 530/395.000
IC      [5]
        ICM: C07K015-06
        ICS: C07K015-14; A61K037-02
EXF     530/350; 530/380; 530/395
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 49 OF 339  USPATFULL
AN      93:76630  USPATFULL
TI      Method to achieve solubilization of spider silk proteins
IN      Lombari, Stephen J., Brighton, MA, United States
        Kaplan, David L., Stow, MA, United States
PA      The United States of America as represented by the Secretary of the
        Army, Washington, DC, United States (U.S. government)
PI      US 5245012              19930914
AI      US 1992-953323          19920929 (7)
RLI     Continuation of Ser. No. US 1990-511114, filed on 19 Apr 1990, now
        abandoned
DT      Utility
FS      Granted
LN.CNT 885
INCL    INCLM: 530/353.000
        INCLS: 530/412.000; 530/422.000; 530/425.000; 008/127.600; 008/128.100
NCL     NCLM:  530/353.000
        NCLS:  008/127.600; 008/128.100; 530/412.000; 530/422.000; 530/425.000
IC      [5]
        ICM: C07K015-20
        ICS: C07K003-00; C07K015-00; C07K015-08
EXF     530/353; 530/412; 530/422; 530/425; 008/127.6; 008/128.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6   ANSWER 50 OF 339  USPATFULL
AN      93:76424  USPATFULL
TI      DNA encoding novel tissue plasminogen activator derivatives having
        kringles 1 and 2 deleted, vectors and host cells
IN      Bang, Nils U., Indianapolis, IN, United States
        Little, Sheila P., Indianapolis, IN, United States
        Schoner, Brigitte E., Zionsville, IN, United States
        Weigel, Barbara J., Indianapolis, IN, United States
PA      Eli Lilly and Company, Indianapolis, IN, United States (U.S.
        corporation)
PI      US 5244806              19930914
AI      US 1990-614966          19901119 (7)
RLI     Continuation of Ser. No. US 1989-348155, filed on 2 May 1989, now
        abandoned which is a continuation of Ser. No. US 1986-889041, filed on
        24 Jul 1986, now abandoned which is a continuation-in-part of Ser. No.
        US 1985-769298, filed on 26 Aug 1985, now abandoned
DT      Utility
FS      Granted
LN.CNT 2723
INCL    INCLM: 435/252.330
        INCLS: 435/226.000; 435/240.200; 435/320.100; 536/023.200; 536/023.400;
               536/023.500
NCL     NCLM:  435/252.330
        NCLS:  435/226.000; 435/320.100; 435/359.000; 536/023.200; 536/023.400;
               536/023.500
IC      [5]
        ICM: C12N009-64
        ICS: C12N009-48; C12N005-00; C12N015-00
EXF     435/219; 435/212; 435/226; 435/320; 435/69.1; 435/172.3; 435/240.2;
        435/252.33; 536/27; 536/23.2; 536/23.4; 536/23.5; 935/4; 935/10; 935/14;
        935/29; 935/32; 935/70; 935/72
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

     (FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
     12:23:48 ON 26 SEP 2002
L1          41608 S ANTIBOD? AND LIBRAR?
L2         137092 S POLYCLONA?
L3          15758 S L2 AND L1
L4           9841 S L3 AND PHAGE?
L5            414 S L4 NOT PY=> 1994
L6            339 DUP REM L5 (75 DUPLICATES REMOVED)

=> s l6 and variabl? (a) region
L7            30 L6 AND VARIABL? (A) REGION

=> d l7 1-30

L7   ANSWER 1 OF 30      MEDLINE
AN   94044806      MEDLINE
DN   94044806    PubMed ID: 8228264
TI   Molecular selection of human antibodies with an unconventional
     bacterial B cell antigen.
AU   Sasano M; Burton D R; Silverman G J
CS   Sam and Rose Stein Institute for Research on Aging, University of
     California, San Diego, La Jolla 92093.
NC   AI00866 (NIAID)
     AI34001 (NIAID)
SO   JOURNAL OF IMMUNOLOGY, (1993 Nov 15) 151 (10) 5822-39.
     Journal code: 2985117R. ISSN: 0022-1767.
CY   United States
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       continuation-in-part of Ser. No. US 1987-111022, filed on 20 Oct 1987
       which is a continuation-in-part of Ser. No. US 1986-922121, filed on 20
       Oct 1986, now abandoned which is a continuation-in-part of Ser. No. US
       1986-847931, filed on 7 Apr 1986, now abandoned which is a
       continuation-in-part of Ser. No. US 1985-725003, filed on 19 Apr 1985,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 1446
INCL   INCLM: 435/240.200
       INCLS: 435/240.250; 530/399.000
NCL    NCLM:  435/378.000
       NCLS:  530/399.000
IC     [5]
       ICM: C12N005-08
       ICS: C07K015-14
EXF    435/240.2; 435/240.21; 435/240.25; 514/2; 514/8; 514/25; 530/395;
       530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 7 OF 30  USPATFULL
AN     93:93905  USPATFULL
TI     Antigenic epitopes present on membrane-bound but not secreted IgE
IN     Chang, Tse-wen, Houston, TX, United States
PA     Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI     US 5260416              19931109
AI     US 1990-468766          19900123 (7)
RLI    Continuation-in-part of Ser. No. US 1989-369625, filed on 21 Jun 1989,
       now abandoned which is a continuation-in-part of Ser. No. US
       1988-272243, filed on 16 Nov 1988, now patented, Pat. No. US 5091313
       which is a continuation-in-part of Ser. No. US 1988-229178, filed on 5
       Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US
       1988-226421, filed on 29 Jul 1988 which is a continuation-in-part of
       Ser. No. US 1987-140036, filed on 31 Dec 1987, now abandoned
DT     Utility
FS     Granted
LN.CNT 859
INCL   INCLM: 530/327.000
       INCLS: 530/387.200; 530/387.300; 530/388.730; 530/862.000; 530/868.000;
              424/085.800
NCL    NCLM:  530/327.000
       NCLS:  424/131.100; 424/139.100; 424/140.100; 424/153.100; 424/805.000;
              424/810.000; 530/387.200; 530/387.300; 530/388.730; 530/862.000;
              530/868.000
IC     [5]
       ICM: C07K007-08
       ICS: C07K017-02
EXF    530/327; 530/388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 8 OF 30  USPATFULL
AN     93:93713  USPATFULL
TI     Methods for detection of human gamma, .gamma. T cell receptor
IN     Brenner, Michael B., Ashland, MA, United States
       Strominger, Jack L., Lexington, MA, United States
       Seidman, John G., Milton, MA, United States
       Ip, Stephen H., Framingham, MA, United States
       Krangel, Michael S., Newtonville, MA, United States
PA     President & Fellows of Harvard College, Boston, MA, United States (U.S.
       corporation)
       Dana Farber Cancer Institute & T Cell Diagnostics, Inc., Boston, MA,
       United States (U.S. corporation)
PI     US 5260223              19931109
AI     US 1988-187698          19880429 (7)
RLI    Continuation-in-part of Ser. No. US 1987-115256, filed on 29 Oct 1987,
       now patented, Pat. No. US 5024940, issued on 18 Jun 1991 which is a
       continuation-in-part of Ser. No. US 1987-16252, filed on 19 Feb 1987
       which is a continuation-in-part of Ser. No. US 1986-882100, filed on 3
       Jul 1986, now abandoned
DT     Utility
FS     Granted
LN.CNT 1745
INCL   INCLM: 436/501.000
       INCLS: 435/007.100; 435/007.240; 435/172.200; 435/240.270; 436/506.000;
              436/518.000; 436/548.000; 436/064.000; 530/387.900; 530/388.220;
              530/388.750; 530/350.000; 536/023.500
NCL    NCLM:  436/501.000
       NCLS:  435/007.100; 435/007.240; 436/064.000; 436/506.000; 436/518.000;
              436/548.000; 530/350.000; 530/387.900; 530/388.220; 530/388.750;
              536/023.500
IC     [5]
       ICM: G01N033-566
EXF    435/7; 435/172.2; 435/240.27; 435/69.6; 435/7.1; 435/7.23; 436/501;
       436/506; 436/518; 436/548; 436/811; 436/813; 436/64; 530/350; 530/387;
       530/395; 530/828; 530/829; 935/110
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 9 OF 30  USPATFULL
AN     93:91541  USPATFULL
TI     DNA encoding and methods of production of insulin-like growth factor
       binding protein BP53
IN     Baxter, Robert C., Plebe, Australia
       Wood, William I., San Mateo, CA, United States
PA     Genentech, Inc., South San Francisco, CA, United States (U.S.
       corporation)
       Central Sydney Area Health Service, Camperdown, Australia (non-U.S.
       corporation)
PI     US 5258287              19931102
AI     US 1988-171623          19880322 (7)
DT     Utility
FS     Granted
LN.CNT 1665
INCL   INCLM: 435/069.100
       INCLS: 536/023.500; 435/006.000; 435/069.800; 435/240.100; 435/240.200;
              435/252.300; 435/254.110; 435/254.200; 435/320.100
NCL    NCLM:  435/069.100
       NCLS:  435/006.000; 435/069.800; 435/252.300; 435/254.110; 435/254.200;
              435/320.100; 435/365.000; 435/369.000; 536/023.500
IC     [5]
       ICM: C12N005-10
       ICS: C12N001-15; C12N001-21; C12N015-12
EXF    435/69.1; 435/6; 435/172.3; 435/69.8; 435/320.1; 435/254; 435/255;
       435/256; 435/240.2; 435/240.1; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 10 OF 30  USPATFULL
AN     93:87456  USPATFULL
TI     Extracellular segments of human e immunoglobulin anchoring peptides and
       antibodies specific therefor
IN     Chang, Tse W., Houston, TX, United States
PA     Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI     US 5254671              19931019
AI     US 1992-973321          19921029 (7)
RLI    Continuation-in-part of Ser. No. US 1990-515604, filed on 27 Apr 1990,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 1331
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DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Abridged Index Medicus Journals; Priority Journals
OS   GENBANK-L19902; GENBANK-L19903; GENBANK-L19904; GENBANK-L19905;
     GENBANK-L19906; GENBANK-L19907; GENBANK-L19908; GENBANK-L19909;
     GENBANK-L19910; GENBANK-L19911; GENBANK-L19912; GENBANK-L19913;
     GENBANK-L19914; GENBANK-L19915; GENBANK-L19916; GENBANK-L19917;
     GENBANK-L19918; GENBANK-L19919; GENBANK-L19920
EM   199312
ED   Entered STN: 19940117
     Last Updated on STN: 19940117
     Entered Medline: 19931210

L7   ANSWER 2 OF 30     MEDLINE
AN   90005436     MEDLINE
DN   90005436   PubMed ID: 2477243
TI   Molecular cloning of the primary IgH repertoire: a quantitative analysis
     of VH gene usage in adult mice.
AU   Sheehan K M; Brodeur P H
CS   Immunology Program, Sackler School of Graduate Biomedical Sciences,
     Boston, MA.
NC   A1-07-77-07 (NIAID)
     P01-AI 23495 (NIGMS)
     RO1-GM 36064
SO   EMBO JOURNAL, (1989 Aug) 8 (8) 2313-20.
     Journal code: 8208664. ISSN: 0261-4189.
CY   ENGLAND: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   198911
ED   Entered STN: 19900328
     Last Updated on STN: 19970203
     Entered Medline: 19891109

L7   ANSWER 3 OF 30  USPATFULL
AN      93:107133  USPATFULL
TI      DNA sequences encoding vascular cell adhesion molecules (VCAMS)
IN      Hession, Catherine A., South Weymouth, MA, United States
        Lobb, Roy R., Westwood, MA, United States
        Goelz, Susan E., Winchester, MA, United States
        Osborn, Laurelee, Brighton, MA, United States
        Benjamin, Christopher D., Beverly, MA, United States
        Rosa, Margaret D., Winchester, MA, United States
PA      Biogen, Inc., Cambridge, MA, United States (U.S. corporation)
PI      US 5272263              19931221
AI      US 1989-452675          19891218 (7)
RLI     Continuation-in-part of Ser. No. US 1989-359516, filed on 1 Jun 1989,
        now abandoned which is a continuation-in-part of Ser. No. US
        1989-345151, filed on 28 Apr 1989
DT      Utility
FS      Granted
LN.CNT 2440
INCL    INCLM: 536/023.500
        INCLS: 530/380.000; 435/069.600; 435/320.100
NCL     NCLM:  536/023.500
        NCLS:  435/069.600; 435/320.100; 530/380.000
IC      [5]
        ICM: C07K013-00
        ICS: C12N015-00; C12P021-06
EXF     435/69.1; 435/69.9; 435/320.1; 530/380; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 4 OF 30  USPATFULL
AN      93:102708  USPATFULL
TI      Mammalian adipocyte protein p154, nucleic acids coding therefor and uses
        thereof
IN      Serrero, Ginette, Lake Placid, NY, United States
PA      W. Alton Jones Cell Science Center, Inc., Lake Placid, NY, United States
        (U.S. corporation)
PI      US 5268295              19931207
AI      US 1991-708038          19910531 (7)
DT      Utility
FS      Granted
LN.CNT 2018
INCL    INCLM: 435/252.300
        INCLS: 435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/172.300;
               435/240.200; 435/320.100; 536/023.500; 935/011.000; 935/027.000;
               935/056.000; 935/066.000
NCL     NCLM:  435/252.300
        NCLS:  435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/320.100;
               536/023.500
IC      [5]
        ICM: C12N015-12
        ICS: C12N015-63
EXF     536/27; 536/23.5; 435/69.1; 435/70.1; 435/70.3; 435/71.1; 435/172.3;
        435/240.2; 435/252.3; 435/320.1; 935/8; 935/11; 935/12; 935/24; 935/27;
        935/56; 935/66
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 5 OF 30  USPATFULL
AN      93:98498  USPATFULL
TI      Platelet cell adhesion molecule and variants thereof
IN      Newman, Peter J., Shorewood, WI, United States
PA      The Blood Center of Southeastern Wisconsin, Inc., Milwaukee, WI, United
        States (U.S. corporation)
PI      US 5264554              19931123
AI      US 1990-466140          19900119 (7)
DT      Utility
FS      Granted
LN.CNT 772
INCL    INCLM: 530/387.100
        INCLS: 530/395.000; 530/350.000; 530/324.000; 435/069.100; 424/085.800
NCL     NCLM:  530/387.100
        NCLS:  435/069.100; 530/324.000; 530/350.000; 530/387.900; 530/395.000;
               536/023.500
IC      [5]
        ICM: C07K013-00
        ICS: C07K009-00; C07K015-14; A61K039-00
EXF     530/387; 530/388; 530/380; 530/395; 530/330; 530/329; 530/328; 530/327;
        530/326; 530/325; 530/324; 530/350; 530/387.1; 514/8; 514/12; 435/69.1;
        424/85.8
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 6 OF 30  USPATFULL
AN      93:96039  USPATFULL
TI      Method for obtaining bone marrow free of tumor cells using transforming
        growth factor .beta.3
IN      Iwata, Kenneth K., Westbury, NY, United States
        Foulkes, J. Gordon, Huntington, NY, United States
        Dijke, Peter T., Port Washington, NY, United States
        Haley, John D., Great Neck, NY, United States
PA      Oncogene Science, Inc., Uniondale, NY, United States (U.S. corporation)
PI      US 5262319              19931116
AI      US 1990-543341          19900625 (7)
RLI     Continuation-in-part of Ser. No. US 1989-353410, filed on 17 May 1989,
        now abandoned which is a continuation-in-part of Ser. No. US
        1988-183824, filed on 20 Apr 1988, now abandoned which is a
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INCL    INCLM: 530/324.000
        INCLS: 530/350.000; 530/386.000; 536/023.530
NCL     NCLM:  530/324.000
        NCLS:  530/350.000; 530/386.000; 536/023.530
IC      [5]
        ICM: C07K007-10
        ICS: C12N015-13
EXF     536/23.23; 536/23.53; 530/324; 530/350; 530/386
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7    ANSWER 11 OF 30  USPATFULL
AN      93:76410  USPATFULL
TI      Expression of recombinant glyoprotein B from herpes simplex virus
IN      Burke, Rae L., San Francisco, CA, United States
        Pachl, Carol, Oakland, CA, United States
        Valenzuela, Pablo D. T., San Francisco, CA, United States
PA      Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI      US 5244792              19930914
AI      US 1990-587179          19900920 (7)
RLI     Continuation of Ser. No. US 1986-921730, filed on 20 Oct 1986, now
        abandoned which is a continuation-in-part of Ser. No. US 1984-597784,
        filed on 6 Apr 1984, now abandoned
DT      Utility
FS      Granted
LN.CNT 1639
INCL    INCLM: 435/069.300
        INCLS: 435/240.200; 435/320.100; 435/069.100; 435/070.300; 435/071.100;
               435/172.300; 435/254.200; 536/023.720; 935/012.000; 935/069.000;
               935/070.000; 424/089.000
NCL     NCLM:  435/069.300
        NCLS:  424/186.100; 424/231.100; 435/069.100; 435/070.300; 435/071.100;
               435/254.200; 435/320.100; 435/362.000; 435/364.000; 435/365.000;
               536/023.720
IC      [5]
        ICM: C12P021-06
        ICS: C12N005-00; C12N015-00; C07H021-00
EXF     435/69.1; 435/69.3; 435/240.2; 435/320.01; 435/255; 435/70.1; 435/70.3;
        435/172.3; 424/88; 935/12; 935/69; 935/70; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7    ANSWER 12 OF 30  USPATFULL
AN      93:61035  USPATFULL
TI      DNA encoding murine-human chimeric antibodies specific for
        antigenic epitopes of IgE present on the extracellular segment of the
        membrane domain of membrane-bound IgE
IN      Chang, Tse W., Houston, TX, United States
PA      Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI      US 5231026              19930727
AI      US 1992-818781          19920106 (7)
RLI     Division of Ser. No. US 1988-272243, filed on 16 Nov 1988, now patented,
        Pat. No. US 5091313 which is a continuation-in-part of Ser. No. US
        1988-229178, filed on 5 Aug 1988, now abandoned which is a
        continuation-in-part of Ser. No. US 1988-226421, filed on 29 Jul 1988,
        now abandoned which is a continuation-in-part of Ser. No. US
        1987-140036, filed on 31 Dec 1987, now abandoned
DT      Utility
FS      Granted
LN.CNT 667
INCL    INCLM: 435/252.300
        INCLS: 435/172.300; 435/320.100; 435/240.270; 435/240.200; 530/387.300;
               530/388.250; 536/023.530
NCL     NCLM:  435/252.300
        NCLS:  435/320.100; 435/328.000; 530/387.300; 530/388.250; 536/023.530
IC      [5]
        ICM: C12N001-20
        ICS: C12N005-10; C12N015-00; C07H015-12
EXF     536/27; 536/172.3; 536/23.53; 435/252.3; 435/252.33; 435/320.1; 435/255;
        435/240.29; 435/240.2; 530/388.25; 530/387.3
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7    ANSWER 13 OF 30  USPATFULL
AN      93:54852  USPATFULL
TI      Lymphocyte homing receptor/immunoglobulin fusion proteins
IN      Capon, Daniel J., San Mateo, CA, United States
        Lasky, Laurence A., Sausalito, CA, United States
PA      Genentech, Inc., South San Francisco, CA, United States (U.S.
        corporation)
PI      US 5225538              19930706
AI      US 1991-808122          19911216 (7)
RLI     Division of Ser. No. US 1989-440625, filed on 22 Nov 1989, now patented,
        Pat. No. US 5116964 which is a continuation of Ser. No. US 1989-315015,
        filed on 23 Feb 1989, now patented, Pat. No. US 5098833
DT      Utility
FS      Granted
LN.CNT 2558
INCL    INCLM: 530/387.300
        INCLS: 435/069.700; 530/388.730
NCL     NCLM:  530/387.300
        NCLS:  424/134.100; 435/069.700; 530/388.730
IC      [5]
        ICM: C07K013-00
        ICS: C17N015-62
EXF     435/69.7; 530/387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7    ANSWER 14 OF 30  USPATFULL
AN      93:52487  USPATFULL
TI      Directed evolution of novel binding proteins
IN      Ladner, Robert C., Ijamsville, MD, United States
        Guterman, Sonia K., Belmont, MA, United States
        Roberts, Bruce L., Milford, MA, United States
        Markland, William, Milford, MA, United States
        Ley, Arthur C., Newton, MA, United States
        Kent, Rachel B., Boxborough, MA, United States
PA      Protein Engineering Corp., Cambridge, MA, United States (U.S.
        corporation)
PI      US 5223409              19930629
AI      US 1991-664989          19910301 (7)
RLI     Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990,
        now abandoned And a continuation-in-part of Ser. No. US 1988-240160,
        filed on 2 Sep 1988, now abandoned
DT      Utility
FS      Granted
LN.CNT 15410
INCL    INCLM: 435/069.700
        INCLS: 435/069.100; 435/172.300; 435/252.300; 435/320.100; 530/380.300;
               530/387.500
NCL     NCLM:  435/069.700
        NCLS:  435/005.000; 435/069.100; 435/252.300; 435/320.100; 435/472.000;
               530/387.300; 530/387.500
IC      [5]
        ICM: C12N015-09
        ICS: C12N015-62; C12N015-63
EXF     435/69.1; 435/172.3; 435/252.3; 435/320.1; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7    ANSWER 15 OF 30  USPATFULL
AN      93:48655  USPATFULL
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TI      Recombinant antibodies and methods for their production in
        which surface residues are altered to cysteine residues for attachment
        of effector or receptor molecules
IN      Bodmer, Mark W., Oxfordshire, United Kingdom
        Adair, John R., High Wycombe, United Kingdom
        Whittle, Nigel R., Surrey, United Kingdom
        Lyons, Alan H., Maidenhead, United Kingdom
        Owens, Raymond J., Henley-on-Thames, United Kingdom
PA      Celltech Limited, Berkshire, United Kingdom (non-U.S. corporation)
PI      US 5219996              19930615
        WO 8901782  19890309
AI      US 1989-353634          19890703 (7)
        WO 1988-GB729           19880905
                                19890703  PCT 371 date
                                19890703  PCT 102(e) date
PRAI    GB 1987-20833       19870904
DT      Utility
FS      Granted
LN.CNT 578
INCL    INCLM: 530/387.300
        INCLS: 530/387.100; 530/391.100; 530/391.500; 424/085.800; 424/085.910;
               435/069.600; 435/070.210; 435/172.200; 435/172.300; 435/240.270;
               435/320.100
NCL     NCLM:  530/387.300
        NCLS:  424/133.100; 424/178.100; 424/801.000; 435/069.600; 435/070.210;
               435/091.410; 435/320.100; 435/466.000; 530/387.100; 530/388.850;
               530/391.100; 530/391.500; 530/867.000; 536/023.530
IC      [5]
        ICM: C07K015-28
        ICS: A61K039-395; C12P021-08
EXF     424/85.8; 424/85.91; 435/69.1; 435/69.6; 435/70.21; 435/172.1;
        435/172.2; 435/172.3; 435/240.27; 435/320.1; 530/387-389; 530/387.1;
        530/387.3; 530/391.5; 530/391.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 16 OF 30  USPATFULL
AN      93:39900  USPATFULL
TI      Genetic material encoding new insulin-like growth factor binding protein
        IGFBP-6
IN      Kiefer, Michael C., Clayton, CA, United States
        Masiarz, Frank R., San Francisco, CA, United States
PA      Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI      US 5212074              19930518
AI      US 1990-576629          19900831 (7)
RLI     Division of Ser. No. US 1990-574613, filed on 28 Aug 1990, now abandoned
DT      Utility
FS      Granted
LN.CNT 1731
INCL    INCLM: 435/069.600
        INCLS: 435/069.100; 435/252.300; 435/240.100; 435/243.000; 435/254.000;
               536/023.500; 935/009.000; 935/011.000; 935/066.000; 530/395.000
NCL     NCLM:  435/069.600
        NCLS:  435/069.100; 435/243.000; 435/252.300; 435/361.000; 530/395.000;
               536/023.500
IC      [5]
        ICM: C12P021-02
        ICS: C07H021-04; C12N001-00
EXF     514/44; 530/303; 530/399; 435/69.1; 435/70.1; 435/71.1; 435/252.3;
        435/252.33; 435/255; 435/240.2; 435/69.5; 435/240.1; 435/240.2;
        435/240.4; 435/254; 435/255; 435/243; 435/69.6; 935/13; 935/9; 800/2;
        536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 17 OF 30  USPATFULL
AN      93:22595  USPATFULL
TI      Characterization of platelet aggregation disorders
IN      Ginsberg, Mark H., San Diego, CA, United States
PA      The Scripps Research Institute, La Jolla, CA, United States (U.S.
        corporation)
PI      US 5196309              19930323
AI      US 1990-614723          19901115 (7)
DT      Utility
FS      Granted
LN.CNT 1855
INCL    INCLM: 435/007.210
        INCLS: 435/007.240; 436/503.000; 436/548.000
NCL     NCLM:  435/007.210
        NCLS:  435/007.240; 436/503.000; 436/548.000
IC      [5]
        ICM: G01N033-567
        ICS: G01N033-577
EXF     435/7.21; 435/7.24; 436/503; 436/548; 436/811; 935/110
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 18 OF 30  USPATFULL
AN      93:10435  USPATFULL
TI      Human .gamma., .delta.T cell antigen receptor polypeptides and nucleic
        acids
IN      Brenner, Michael B., Sherborn, MA, United States
        Seidman, Jonathan, Milton, MA, United States
        Strominger, Jack L., Lexington, MA, United States
        Ip, Stephen H., Sudbury, MA, United States
        Krangel, Michael S., Chapel Hill, NC, United States
        Band, Hamid, Boston, MA, United States
PA      T Cell Sciences, Inc., Cambridge, MA, United States (U.S. corporation)
        Dana Farber Cancer Institute, Boston, MA, United States (U.S.
        corporation)
        President & Fellows of Harvard College, Boston, MA, United States (U.S.
        corporation)
PI      US 5185250              19930209
AI      US 1989-297661          19890113 (7)
RLI     Continuation-in-part of Ser. No. US 1988-187698, filed on 29 Apr 1988
        which is a continuation-in-part of Ser. No. US 1987-115256, filed on 29
        Oct 1987, now patented, Pat. No. US 5024940 which is a
        continuation-in-part of Ser. No. US 1987-16252, filed on 19 Feb 1987
        which is a continuation-in-part of Ser. No. US 1986-882100, filed on 3
        Jul 1986, now abandoned
DT      Utility
FS      Granted
LN.CNT 5332
INCL    INCLM: 435/069.300
        INCLS: 435/069.100; 435/007.240; 435/172.200; 435/240.270; 530/350.000;
               530/387.900; 530/388.220; 530/388.750; 536/023.500
NCL     NCLM:  435/069.300
        NCLS:  435/007.240; 435/069.100; 530/350.000; 530/387.900; 530/388.220;
               530/388.750; 536/023.500
IC      [5]
        ICM: C12P021-06
        ICS: C12N005-02; A61K035-14; C07H015-12
EXF     435/7; 435/69.1; 435/172.2; 435/172.3; 435/68.1; 435/70; 435/6;
        435/240.27; 435/69.3; 536/27; 530/387; 530/359
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 19 OF 30  USPATFULL
AN      93:5468  USPATFULL
TI      Versican core protein, nucleic acid sequences encoding the same, nucleic
        acid probes, anti-versican antibodies, and methods of
        detecting the same
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IN      Ruoslahti, Erkki I., Rancho Santa Fe, CA, United States
PA      La Jolla Cancer Research Foundation, La Jolla, CA, United States (U.S.
        corporation)
PI      US 5180808              19930119
AI      US 1989-441179          19891127 (7)
DT      Utility
FS      Granted
LN.CNT 559
INCL    INCLM: 530/350.000
        INCLS: 530/387.900; 530/388.200; 530/389.100; 536/023.500
NCL     NCLM:  530/350.000
        NCLS:  530/387.900; 530/388.200; 530/389.100; 536/023.500
IC      [5]
        ICM: C07K003-00
        ICS: C07H015-12
EXF     436/561; 436/23; 436/503; 436/519; 536/27; 530/350; 530/387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 20 OF 30  USPATFULL
AN      92:84786  USPATFULL
TI      Method of producing secreted receptor analogs and biologically active
        peptide dimers
IN      Sledziewski, Andrzej Z., Seattle, WA, United States
        Bell, Lillian A., Seattle, WA, United States
        Kindsvogel, Wayne R., Seattle, WA, United States
PA      ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI      US 5155027              19921013
AI      US 1989-347291          19890502 (7)
PRAI    EP 1989-100787      19890118
DT      Utility
FS      Granted
LN.CNT 2238
INCL    INCLM: 435/069.700
        INCLS: 435/172.300; 530/387.300; 530/350.000; 530/388.220
NCL     NCLM:  435/069.700
        NCLS:  435/483.000; 530/350.000; 530/388.220; 530/389.300
IC      [5]
        ICM: C12N015-62
EXF     435/68; 435/70; 435/235; 435/320; 435/243; 435/253; 435/272; 435/240.27;
        435/240.2; 435/240.1; 435/69.1; 435/69.7; 435/172.3; 530/356; 530/387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 21 OF 30  USPATFULL
AN      92:72459  USPATFULL
TI      Method and means for extending the host range of insecticidal proteins
IN      Sivasubramanian, Natarajan, Riverside, CA, United States
        Federici, Brian A., Riverside, CA, United States
PA      The Regents of the University of California, Oakland, CA, United States
        (U.S. corporation)
PI      US 5143905              19920901
AI      US 1990-518575          19900503 (7)
DT      Utility
FS      Granted
LN.CNT 1364
INCL    INCLM: 514/021.000
        INCLS: 514/008.000; 514/012.000; 530/350.000; 530/409.000; 424/405.000;
               435/069.700
NCL     NCLM:  514/021.000
        NCLS:  424/405.000; 435/069.700; 514/008.000; 514/012.000; 530/350.000;
               530/409.000
IC      [5]
        ICM: C07K003-08
        ICS: A61K037-00; A61K039-07; A61K039-12
EXF     530/350; 530/409; 514/21; 514/8; 514/12; 424/405

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 22 OF 30  USPATFULL
AN      92:70238  USPATFULL
TI      Marker for early detection of human hydatidiform moles and
        choriocarcinomas
IN      Chou, Janice, Potomac, MD, United States
PA      The United States of America as represented by the Department of Health
        and Human Services, Washington, DC, United States (U.S. government)
PI      US 5141849              19920825
AI      US 1990-536101          19900608 (7)
DT      Utility
FS      Granted
LN.CNT 669
INCL    INCLM: 435/006.000
        INCLS: 435/007.100; 435/810.000; 536/026.000; 536/027.000; 536/028.000;
               536/029.000; 530/326.000; 530/328.000; 530/387.900; 530/388.200;
               530/388.850; 530/389.100; 530/389.700; 935/077.000; 935/078.000;
               436/501.000; 436/094.000
NCL     NCLM:  435/006.000
        NCLS:  435/007.100; 435/810.000; 436/501.000; 530/326.000; 530/328.000;
               530/387.900; 530/388.200; 530/388.850; 530/389.100; 530/389.700;
               536/023.500; 536/024.310
IC      [5]
        ICM: C12Q001-68
        ICS: G01N033-53; A61K037-02; C07H015-12
EXF     536/26; 536/27; 536/28; 435/6; 435/7.1; 435/7.23; 530/328; 530/326;
        530/387; 935/77; 935/78
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 23 OF 30  USPATFULL
AN      92:42890  USPATFULL
TI      Hybrid immunoglobulins
IN      Capon, Daniel J., San Mateo, CA, United States
        Lasky, Laurence A., Sausalito, CA, United States
PA      Genentech, Inc., South San Francisco, CA, United States (U.S.
        corporation)
PI      US 5116964              19920526
AI      US 1989-440625          19891122 (7)
RLI     Continuation-in-part of Ser. No. US 1989-315015, filed on 23 Feb 1989
DT      Utility
FS      Granted
LN.CNT 2533
INCL    INCLM: 536/027.000
        INCLS: 435/069.700; 435/252.300; 435/320.110; 530/350.000
NCL     NCLM:  536/023.500
        NCLS:  424/134.100; 435/069.700; 435/252.300; 435/320.100; 530/350.000;
               530/387.300; 536/023.510; 536/023.530
IC      [5]
        ICM: C07H021-04
        ICS: C12N015-62; C12P021-02
EXF     435/69.7; 435/172.3; 435/252.3; 435/320; 436/512; 530/350; 530/387;
        536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 24 OF 30  USPATFULL
AN      92:36291  USPATFULL
TI      Derivatives of soluble T-4
IN      Maddon, Paul J., New York, NY, United States
        Axel, Richard, New York, NY, United States
        Sweet, Raymond W., Bala Cynwyd, PA, United States
        Arthos, James, Ann Arbor, MI, United States
PA      The Trustees of Columbia University in the City of New York, New York,
        NY, United States (U.S. corporation)
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       Smithkline Beckman Corporation, Philadelphia, PA, United States (U.S.
       corporation)
PI     US 5110906               19920505
AI     US 1988-160348           19880224 (7)
RLI    Continuation-in-part of Ser. No. US 1987-114244, filed on 23 Oct 1987
       which is a continuation-in-part of Ser. No. US 1986-898587, filed on 21
       Aug 1986, now abandoned
DT     Utility
FS     Granted
LN.CNT 2771
INCL   INCLM: 530/350.000
       INCLS: 435/005.000; 435/974.000; 530/395.000; 530/829.000; 930/221.000
NCL    NCLM:  530/350.000
       NCLS:  435/005.000; 435/974.000; 530/395.000; 530/821.000; 930/221.000
IC     [5]
       ICM: C07K013-00
EXF    530/387; 530/395; 530/350; 530/829; 930/221; 435/5; 435/974
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 25 OF 30  USPATFULL
AN     92:3765  USPATFULL
TI     Interleukin-1 receptors
IN     Dower, Steven K., Redmond, WA, United States
       March, Carl J., Seattle, WA, United States
       Sims, John E., Seattle, WA, United States
       Urdal, David L., Seattle, WA, United States
PA     Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI     US 5081228               19920114
AI     US 1988-258756           19881013 (7)
RLI    Continuation-in-part of Ser. No. US 1988-160550, filed on 25 Feb 1988,
       now patented, Pat. No. US 4968607 which is a continuation-in-part of
       Ser. No. US 1987-125627, filed on 25 Nov 1987, now abandoned
DT     Utility
FS     Granted
LN.CNT 1540
INCL   INCLM: 530/035.100
       INCLS: 530/350.000; 530/395.000; 530/820.000; 435/069.500; 435/069.100;
              424/085.100; 424/085.200; 514/002.000; 514/008.000
NCL    NCLM:  530/351.000
       NCLS:  424/085.100; 424/085.200; 435/069.100; 435/069.500; 514/002.000;
              514/008.000; 530/350.000; 530/395.000; 530/820.000
IC     [5]
       ICM: C07K013-00
       ICS: A61K037-02
EXF    530/351; 530/350; 530/395; 530/820; 435/68; 435/70; 514/2; 514/8;
       424/85.1; 424/85.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 26 OF 30  USPATFULL
AN     91:42649  USPATFULL
TI     Synovial phospholipases
IN     Johnson, Lorin K., Pleasanton, CA, United States
       Seilhamer, Jeffrey J., Milpitas, CA, United States
       Pruzanski, Waldemar, Ontario, Canada
       Vadas, Peter, Ontario, Canada
PA     Biotechnology Research Partners, Ltd., Ontario, CA, United States (U.S.
       corporation)
       The University of Toronto Innovations Foundation, Ontario, Canada
       (non-U.S. corporation)
PI     US 5019508               19910528
AI     US 1988-215726           19880706 (7)
RLI    Continuation-in-part of Ser. No. US 1987-89883, filed on 27 Aug 1987,
       now abandoned
DT     Utility
FS     Granted
LN.CNT 1397
INCL   INCLM: 435/198.000
       INCLS: 435/172.100; 435/320.100; 435/252.300; 536/027.000; 935/014.000
NCL    NCLM:  435/198.000
       NCLS:  435/252.300; 435/320.100; 536/023.200; 536/023.500
IC     [5]
       ICM: C12N009-20
       ICS: C12N015-55; C07H015-12
EXF    435/172.3; 435/198; 435/320; 435/240.2; 435/252.3; 435/235; 435/255;
       935/14; 935/28; 935/29; 935/31; 935/56; 935/58; 935/69; 935/71; 935/72;
       536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 27 OF 30  USPATFULL
AN     90:85544  USPATFULL
TI     Interleukin-1 receptors
IN     Dower, Steven K., Redmond, WA, United States
       March, Carl J., Seattle, WA, United States
       Sims, John E., Seattle, WA, United States
       Urdal, David L., Seattle, WA, United States
PA     Immunex Corporation, Seattle, WA, United States (U.S. corporation)
PI     US 4968607               19901106
AI     US 1988-160550           19880225 (7)
RLI    Continuation-in-part of Ser. No. US 1987-125627, filed on 25 Nov 1987
DT     Utility
FS     Granted
LN.CNT 1513
INCL   INCLM: 435/069.100
       INCLS: 536/027.000; 435/320.000; 435/235.000; 435/240.100; 435/252.800;
              435/255.000; 330/387.000; 330/399.000
NCL    NCLM:  435/069.100
       NCLS:  435/235.100; 435/252.800; 530/388.220; 530/399.000; 536/023.500;
              536/023.510; 536/024.310
IC     [5]
       ICM: C12N015-00
       ICS: C12N015-12; C12N012-11; C12N000-6
EXF    536/27; 435/68; 435/172.3; 435/235; 435/320; 435/240.1; 435/69.1;
       435/252.8; 435/255; 530/387; 530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 28 OF 30  USPATFULL
AN     90:76640  USPATFULL
TI     Compositions and methods for the synthesis and assay of a mammalian
       enkephalinase
IN     Malfroy-Camine, Bernard, San Bruno, CA, United States
       Schofield, Peter R., San Francisco, CA, United States
PA     Genentech, Inc., So. San Francisco, CA, United States (U.S. corporation)
PI     US 4960700               19901002
AI     US 1987-2478             19870112 (7)
RLI    Continuation-in-part of Ser. No. US 1986-946566, filed on 24 Dec 1986
DT     Utility
FS     Granted
LN.CNT 1420
INCL   INCLM: 435/172.300
       INCLS: 435/212.000; 435/219.000; 435/240.200; 435/252.330; 435/071.100;
              435/091.000; 435/172.100; 435/172.300; 435/320.000; 536/027.000;
              530/350.000; 935/018.000; 935/019.000; 935/031.000; 935/041.000;
              935/058.000; 935/070.000; 935/073.000; 935/082.000
NCL    NCLM:  435/219.000
       NCLS:  435/212.000; 435/252.330; 435/358.000; 435/369.000
IC     [5]
       ICM: C12N009-48
       ICS: C12N009-50; C12N005-00; C12N001-22; C12N015-00; C12N001-00;
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        C12P021-04; C12P019-34; C07H015-12; C07K013-00
EXF     435/68; 435/70; 435/91; 435/172.1; 435/172.3; 435/219; 435/212; 530/350;
        935/19; 935/34; 935/70
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 29 OF 30  USPATFULL
AN      89:98909  USPATFULL
TI      Diagnostic reagents based on unique sequences within the
        variable region of the T cell receptor and uses
        thereof
IN      Hood, Leroy E., Pasadena, CA, United States
        Weissman, Irving L., Stanford, CA, United States
        McGrath, Michael S., Menlo Park, CA, United States
PA      California Institute of Technology, Pasadena, CA, United States (U.S.
        corporation)
PI      US 4886743              19891212
AI      US 1985-726502          19850424 (6)
DT      Utility
FS      Granted
LN.CNT 1777
INCL    INCLM: 435/005.000
        INCLS: 435/006.000; 435/007.000; 435/029.000; 530/387.000; 530/326.000;
               935/078.000; 935/104.000; 935/011.000; 935/012.000; 436/548.000;
               436/813.000; 436/536.000; 436/052.000; 436/063.000; 436/506.000;
               436/508.000; 436/509.000
NCL     NCLM:  435/005.000
        NCLS:  435/006.000; 435/007.220; 435/007.230; 435/007.240; 435/029.000;
               435/188.000; 435/974.000; 436/052.000; 436/063.000; 436/506.000;
               436/508.000; 436/509.000; 436/536.000; 436/548.000; 436/813.000;
               530/326.000; 530/387.900; 530/388.220; 530/388.750; 530/388.900;
               530/389.100; 530/389.600; 530/389.800; 530/391.300; 536/024.300
IC      [4]
        ICM: C12Q001-68
        ICS: G01N033-53; G01N033-569; C07K007-10
EXF     435/5-7; 435/29; 435/810; 436/501; 436/503; 436/504; 436/506; 436/508;
        436/509; 436/518; 436/536; 436/548; 436/813; 436/820; 436/52; 436/63;
        935/11; 935/12; 935/78; 935/25; 935/80; 935/81; 935/104; 530/326;
        530/387; 530/388; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7   ANSWER 30 OF 30  USPATFULL
AN      89:23522  USPATFULL
TI      Recombinant immunoglobin preparations
IN      Cabilly, Shmuel, Monrovia, CA, United States
        Heyneker, Herbert L., Burlingame, CA, United States
        Holmes, William E., Pacifica, CA, United States
        Riggs, Arthur D., La Verne, CA, United States
        Wetzel, Ronald B., San Francisco, CA, United States
PA      Genentech, Inc., South San Francisco, CA, United States (U.S.
        corporation)
PI      US 4816567              19890328
AI      US 1983-483457          19830408 (6)
DT      Utility
FS      Granted
LN.CNT 1669
INCL    INCLM: 530/387.000
        INCLS: 435/068.000; 435/172.300; 435/320.000; 435/252.300; 435/252.310;
               435/252.330; 435/252.340; 935/010.000; 935/015.000; 935/029.000;
               935/073.000; 530/388.000
NCL     NCLM:  530/387.300
        NCLS:  435/069.600; 435/252.300; 435/252.310; 435/252.330; 435/252.340;
               435/320.100; 435/471.000; 530/388.850; 530/866.000; 530/867.000;
               930/010.000; 930/300.000
IC      [4]
        ICM: C07K015-14
        ICS: C07K015-06; C12P021-00; C12N015-00; C12N001-20
EXF     435/68; 435/172.3; 435/240; 435/253; 435/172.2; 435/317; 435/320;
        260/112B; 536/27; 935/11; 935/15; 935/27; 935/29; 935/73; 530/387;
        530/388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d his

     (FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
     12:23:48 ON 26 SEP 2002
L1          41608 S ANTIBOD? AND LIBRAR?
L2         137092 S POLYCLONA?
L3          15758 S L2 AND L1
L4           9841 S L3 AND PHAGE?
L5            414 S L4 NOT PY=> 1994
L6            339 DUP REM L5 (75 DUPLICATES REMOVED)
L7             30 S L6 AND VARIABL? (A) REGION

=> s antibod (a) librar?
L8              0 ANTIBOD (A) LIBRAR?

=> s antibod?(a)librar?
L9           1668 ANTIBOD?(A) LIBRAR?

=> s 19 and polyclon?
L10           628 L9 AND POLYCLON?

=> s 110 not py=
MISSING TERM AFTER PY=
Operators must be followed by a search term, L-number, or query name.

=> s 1110 not py=>1994
L110 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s 110 not py=> 1994
'1994' NOT A VALID FIELD CODE
   5 FILES SEARCHED...
L11             1 L10 NOT PY=> 1994

=> d 111

L11  ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   1988:177831  BIOSIS
DN   BA85:89933
TI   MOLECULE CLONING AND AMINO ACID SEQUENCE OF HUMAN 5 LIPOXYGENASE.
AU   MATSUMOTO T; FUNK C D; RADMARK O; HOOG J-O; JORNVALL H; SAMUELSSON B
CS   CENTRAL RES. INST., JAPAN TOBACCO, INC., MIDORI-KU, YOKOHAMA, JPN.
SO   PROC NATL ACAD SCI U S A, (1988) 85 (1), 26-30.
     CODEN: PNASA6. ISSN: 0027-8424.
FS   BA; OLD
LA   English


=> d his

     (FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
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     12:23:48 ON 26 SEP 2002
L1         41608 S ANTIBOD? AND LIBRAR?
L2        137092 S POLYCLONA?
L3         15758 S L2 AND L1
L4          9841 S L3 AND PHAGE?
L5           414 S L4 NOT PY=> 1994
L6           339 DUP REM L5 (75 DUPLICATES REMOVED)
L7            30 S L6 AND VARIABL? (A) REGION
L8             0 S ANTIBOD (A) LIBRAR?
L9          1668 S ANTIBOD?(A)LIBRAR?
L10          628 S L9 AND POLYCLON?
L11            1 S L10 NOT PY=> 1994

=> dup rem l10
PROCESSING COMPLETED FOR L10
L12          599 DUP REM L10 (29 DUPLICATES REMOVED)

=> s l12 and nucleic(a)acid(a) segment?
L13           48 L12 AND NUCLEIC(A) ACID(A) SEGMENT?

=> d 1-48

L13  ANSWER 1 OF 48  USPATFULL
AN     2002:251931  USPATFULL
TI     Stress resistant retroviruses
IN     Soong, Nay Wei, San Jose, CA, UNITED STATES
       Stemmer, Willem P.C., Los Gatos, CA, UNITED STATES
       Powell, Sharon K., Alameda, CA, UNITED STATES
       Otto, Edward, Falls Church, VA, UNITED STATES
PI     US 2002137889       A1   20020926
AI     US 2001-954983      A1   20010917 (9)
PRAI   US 2000-233398P     20000918 (60)
DT     Utility
FS     APPLICATION
LN.CNT 4898
INCL   INCLM: 530/350.000
       INCLS: 435/235.100; 435/069.100; 435/325.000; 536/023.720
NCL    NCLM:  530/350.000
       NCLS:  435/235.100; 435/069.100; 435/325.000; 536/023.720
IC     [7]
       ICM: C12N007-01
       ICS: C12P021-02; C07H021-04; C07K014-15; C12N005-06

L13  ANSWER 2 OF 48  USPATFULL
AN     2002:251101  USPATFULL
TI     Novel nucleic acids and polypeptides
IN     Tang, Y. Tom, San Jose, CA, UNITED STATES
       Zhou, Ping, Cupertino, CA, UNITED STATES
       Goodrich, Ryle, San Jose, CA, UNITED STATES
       Liu, Chenghua, San Jose, CA, UNITED STATES
       Asundi, Vinod, Foster City, CA, UNITED STATES
       Wehrman, Tom, Stanford, CA, UNITED STATES
       Yang, Yonghong, San Jose, CA, UNITED STATES
       Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
PI     US 2002137044       A1   20020926
AI     US 2001-774434      A1   20010130 (9)
RLI    Continuation-in-part of Ser. No. US 2000-560875, filed on 27 Apr 2000,
       PENDING Continuation-in-part of Ser. No. US 2000-496914, filed on 3 Feb
       2000, ABANDONED
DT     Utility
FS     APPLICATION
LN.CNT 5858
INCL   INCLM: 435/006.000
       INCLS: 536/023.100; 530/324.000; 530/387.900; 435/007.100; 435/069.100;
              514/002.000; 424/130.100
NCL    NCLM:  435/006.000
       NCLS:  536/023.100; 530/324.000; 530/387.900; 435/007.100; 435/069.100;
              514/002.000; 424/130.100
IC     [7]
       ICM: A01N037-18
       ICS: A61K038-00; C12Q001-68; G01N033-53; C07H021-02; C07H021-04;
       C12P021-06; A61K039-395; C07K005-00; C07K007-00; C07K016-00; C07K017-00;
       C12P021-08

L13  ANSWER 3 OF 48  USPATFULL
AN     2002:246560  USPATFULL
TI     Methods and compositions for inhibiting neoplastic cell growth
IN     Edwards, Jean-Baptiste Dumas Milne, Paris, FRANCE
       Duclert, Aymeric, Saint-Maur, FRANCE
       Bougueleret, Lydie, PetitLancy, SWITZERLAND
       Clusel, Catherine, Montreuil-sous-Bois, FRANCE
PA     Genset S.A., Paris, FRANCE (non-U.S. corporation)
PI     US 6455280          B1   20020924
AI     US 2000-750580           20001228 (9)
RLI    Continuation-in-part of Ser. No. US 2000-599362, filed on 21 Jun 2000
       Continuation-in-part of Ser. No. WO 2000-IB1011, filed on 21 Jun 2000
       Continuation-in-part of Ser. No. US 1999-469099, filed on 21 Dec 1999
       Continuation-in-part of Ser. No. WO 1999-IB2058, filed on 20 Dec 1999
PRAI   US 1999-141032P     19990625 (60)
       US 1998-113686P     19981222 (60)
DT     Utility
FS     GRANTED
LN.CNT 10937
INCL   INCLM: 435/069.100
       INCLS: 435/320.100; 530/350.000; 530/412.000; 530/417.000; 530/418.000;
              536/023.100; 536/023.500
NCL    NCLM:  435/069.100
       NCLS:  435/320.100; 530/350.000; 530/412.000; 530/417.000; 530/418.000;
              536/023.100; 536/023.500
IC     [7]
       ICM: C07K001-00
       ICS: C07K014-00; C07K017-00; C12N015-00; C12N015-09; C12N015-63;
       C12N015-70; C12N015-74; C12P021-06; A23J001-00; C07H021-04
EXF    530/350; 530/412; 530/417; 530/418; 435/320.1; 435/69.1; 536/23.1;
       536/23.5

L13  ANSWER 4 OF 48  USPATFULL
AN     2002:243064  USPATFULL
TI     EGF motif protein, EGFL6 materials and methods
IN     Ford, John E., San Diego, CA, UNITED STATES
       Yeung, George, Mountain View, CA, UNITED STATES
       Zhou, Hua, Santa Clara, CA, UNITED STATES
PI     US 2002132250       A1   20020919
AI     US 2001-981649      A1   20011015 (9)
RLI    Continuation-in-part of Ser. No. US 2000-687860, filed on 13 Oct 2000,
       PENDING Continuation-in-part of Ser. No. US 1999-363316, filed on 28 Jul
       1999, GRANTED, Pat. No. US 6392019
DT     Utility
FS     APPLICATION
LN.CNT 5958
INCL   INCLM: 435/006.000
       INCLS: 536/023.200
NCL    NCLM:  435/006.000
       NCLS:  536/023.200
IC     [7]
       ICM: C12Q001-68
       ICS: C07H021-04
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L13  ANSWER 5 OF 48  USPATFULL
AN     2002:243051  USPATFULL
TI     Compositions and methods for the therapy and diagnosis of ovarian cancer
IN     Algate, Paul A., Issaquah, WA, UNITED STATES
       Jones, Robert, Seattle, WA, UNITED STATES
       Harlocker, Susan L., Seattle, WA, UNITED STATES
PA     Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation)
PI     US 2002132237       A1   20020919
AI     US 2001-867701      A1   20010529 (9)
PRAI   US 2000-207484P      20000526 (60)
DT     Utility
FS     APPLICATION
LN.CNT 25718
INCL   INCLM: 435/006.000
       INCLS: 435/091.200
NCL    NCLM:  435/006.000
       NCLS:  435/091.200
IC     [7]
       ICM: C12Q001-68
       ICS: C12P019-34

L13  ANSWER 6 OF 48  USPATFULL
AN     2002:235990  USPATFULL
TI     Novel nucleic acids and polypeptides
IN     Tang, Y. Tom, San Jose, CA, UNITED STATES
       Zhou, Ping, Cupertino, CA, UNITED STATES
       Goodrich, Ryle, San Jose, CA, UNITED STATES
       Liu, Chenghua, San Jose, CA, UNITED STATES
       Asundi, Vinod, Foster City, CA, UNITED STATES
       Ren, Feiyan, Cupertino, CA, UNITED STATES
       Zhao, Qing A., San Jose, CA, UNITED STATES
       Yang, Yonghong, San Jose, CA, UNITED STATES
       Wehrman, Tom, Stanford, CA, UNITED STATES
       Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
PI     US 2002128187       A1   20020912
AI     US 2000-728422      A1   20001130 (9)
RLI    Continuation-in-part of Ser. No. US 2000-560875, filed on 27 Apr 2000,
       PENDING Continuation-in-part of Ser. No. US 2000-496914, filed on 3 Feb
       2000, ABANDONED
DT     Utility
FS     APPLICATION
LN.CNT 5355
INCL   INCLM: 514/012.000
       INCLS: 530/350.000; 536/023.500; 435/069.100; 435/325.000; 435/320.100
NCL    NCLM:  514/012.000
       NCLS:  530/350.000; 536/023.500; 435/069.100; 435/325.000; 435/320.100
IC     [7]
       ICM: A61K038-17
       ICS: C07K014-705; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 7 OF 48  USPATFULL
AN     2002:235016  USPATFULL
TI     Novel nucleic acids and polypeptides
IN     Tang, Y. Tom, San Jose, CA, UNITED STATES
       Zhou, Ping, Cupertino, CA, UNITED STATES
       Goodrich, Ryle, San Jose, CA, UNITED STATES
       Asundi, Vinod, Foster City, CA, UNITED STATES
       Yang, Yonghong, San Jose, CA, UNITED STATES
       Zhang, Jie, Campbell, CA, UNITED STATES
       Wehrman, Tom, Stanford, CA, UNITED STATES
       Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
PI     US 2002127199       A1   20020912
AI     US 2001-815925      A1   20010322 (9)
RLI    Continuation-in-part of Ser. No. US 2000-560875, filed on 27 Apr 2000,
       PENDING Continuation-in-part of Ser. No. US 2000-496914, filed on 3 Feb
       2000, ABANDONED
DT     Utility
FS     APPLICATION
LN.CNT 6503
INCL   INCLM: 424/085.100
       INCLS: 435/006.000; 435/007.100; 435/069.500; 435/325.000; 435/320.100;
              530/351.000; 536/023.100
NCL    NCLM:  424/085.100
       NCLS:  435/006.000; 435/007.100; 435/069.500; 435/325.000; 435/320.100;
              530/351.000; 536/023.100
IC     [7]
       ICM: C12Q001-68
       ICS: G01N033-53; C07H021-04; C12P021-02; C12N005-06; A61K038-19
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 8 OF 48  USPATFULL
AN     2002:230849  USPATFULL
TI     Receptor-mediated gene delivery using bacteriophage vectors
IN     Larocca, David, Encinitas, CA, United States
       Baird, Andrew, San Diego, CA, United States
       Johnson, Wendy, Encinitas, CA, United States
PA     Selective Genetics, Inc., San Diego, CA, United States (U.S.
       corporation)
PI     US 6448083          B1     20020910
AI     US 1999-258584             19990226 (9)
RLI    Continuation-in-part of Ser. No. WO 1998-US17950, filed on 28 Aug 1998
       Continuation-in-part of Ser. No. US 1997-920396, filed on 29 Aug 1997,
       now patented, Pat. No. US 6054312
DT     Utility
FS     GRANTED
LN.CNT 2896
INCL   INCLM: 435/456.000
       INCLS: 435/320.100
NCL    NCLM:  435/456.000
       NCLS:  435/320.100
IC     [7]
       ICM: C12N015-64
       ICS: C12N015-63
EXF    435/456; 435/320.1

L13  ANSWER 9 OF 48  USPATFULL
AN     2002:230601  USPATFULL
TI     Methods and materials relating to novel CD39-like polypeptides
IN     Ford, John, San Mateo, CA, United States
       Mulero, Julio J., Palo Alto, CA, United States
       Yeung, George, San Mateo, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6447771          B1     20020910
AI     US 1999-370265             19990809 (9)
RLI    Continuation-in-part of Ser. No. WO 1999-US16180, filed on 16 Jul 1999
       Continuation-in-part of Ser. No. US 1999-350836, filed on 9 Jul 1999,
       now patented, Pat. No. US 6387645 Continuation-in-part of Ser. No. US
       1999-273447, filed on 19 Mar 1999, now abandoned
DT     Utility
FS     GRANTED
LN.CNT 4376
INCL   INCLM: 424/094.610
NCL    NCLM:  424/094.610
IC     [7]
       ICM: A61K038-47
EXF    435/13; 435/18; 435/269; 435/267; 435/270; 424/94.61
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L13  ANSWER 10 OF 48  USPATFULL
AN      2002:224704  USPATFULL
TI      CTLA4-C.gamma.4 fusion proteins
IN      Gray, Gary S., Brookline, MA, United States
        Carson, Jerry, Belmont, MA, United States
        Javaherian, Kashi, Lexington, MA, United States
        Rennert, Paul D., Holliston, MA, United States
        Silver, Sandra, Boston, MA, United States
PA      Repligen Corporation, Needham, MA, United States (U.S. corporation)
PI      US 6444792          B1   20020903
AI      US 1999-227595           19990108 (9)
RLI     Division of Ser. No. US 1996-595590, filed on 2 Feb 1996
DT      Utility
FS      GRANTED
LN.CNT 3031
INCL    INCLM: 530/387.300
        INCLS: 530/387.100; 424/134.100
NCL     NCLM:  530/387.300
        NCLS:  530/387.100; 424/134.100
IC      [7]
        ICM: A61K039-395
EXF     530/387.1; 530/387.3; 530/388.8; 530/388.85; 424/134.1; 424/155.1;
        424/157.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 11 OF 48  USPATFULL
AN      2002:221018  USPATFULL
TI      Antibody conjugate formulations for selectively inhibiting VEGF
IN      Thorpe, Philip E., Dallas, TX, UNITED STATES
        Brekken, Rolf A., Seattle, WA, UNITED STATES
PA      Board of Regents,The University of Texas System (U.S. corporation)
PI      US 2002119153       A1   20020829
AI      US 2001-998831      A1   20011130 (9)
RLI     Continuation of Ser. No. US 2000-561108, filed on 28 Apr 2000, PATENTED
PRAI    US 1999-131432P      19990428 (60)
DT      Utility
FS      APPLICATION
LN.CNT 10502
INCL    INCLM: 424/145.100
        INCLS: 530/388.240; 424/133.100
NCL     NCLM:  424/145.100
        NCLS:  530/388.240; 424/133.100
IC      [7]
        ICM: A61K039-395
        ICS: C07K016-22
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 12 OF 48  USPATFULL
AN      2002:214215  USPATFULL
TI      Human beta-defensin-3 (HBD-3), a highly cationic beta-defensin
        antimicrobial peptide
IN      McCray, Paul B., JR., Iowa City, IA, UNITED STATES
        Tack, Brian F., Iowa City, IA, UNITED STATES
        Jia, Hong Peng, Iowa City, IA, UNITED STATES
        Schutte, Brian C., Iowa City, IA, UNITED STATES
PI      US 2002115602       A1   20020822
AI      US 2001-872852      A1   20010601 (9)
PRAI    US 2000-208792P      20000601 (60)
DT      Utility
FS      APPLICATION
LN.CNT 3851
INCL    INCLM: 514/012.000
        INCLS: 530/324.000
NCL     NCLM:  514/012.000
        NCLS:  530/324.000
IC      [7]
        ICM: A61K038-17
        ICS: C07K014-435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 13 OF 48  USPATFULL
AN      2002:213441  USPATFULL
TI      CTLA4-Cgamma4 fusion proteins
IN      Gray, Gary S., Brookline, MA, UNITED STATES
        Carson, Jerry, Belmont, MA, UNITED STATES
        Javaherian, Kashi, Lexington, MA, UNITED STATES
        Rennert, Paul D., Holliston, MA, UNITED STATES
        Silver, Sandra, Boston, MA, UNITED STATES
PI      US 2002114814       A1   20020822
AI      US 2001-27075       A1   20011220 (10)
RLI     Continuation of Ser. No. US 1999-227595, filed on 8 Jan 1999, PENDING
        Division of Ser. No. US 1996-595590, filed on 2 Feb 1996, PENDING
DT      Utility
FS      APPLICATION
LN.CNT 3341
INCL    INCLM: 424/178.100
        INCLS: 536/023.530; 435/069.100; 435/326.000; 435/320.100; 530/388.220
NCL     NCLM:  424/178.100
        NCLS:  536/023.530; 435/069.100; 435/326.000; 435/320.100; 530/388.220
IC      [7]
        ICM: A61K039-395
        ICS: C07H021-04; C12P021-02; A61K039-44; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 14 OF 48  USPATFULL
AN      2002:209359  USPATFULL
TI      Nucleic acids and polypeptides
IN      Tang, Y. Tom, San Jose, CA, United States
        Liu, Chenghua, San Jose, CA, United States
        Zhou, Ping, San Jose, CA, United States
        Asundi, Vinod, Foster City, CA, United States
        Zhang, Jie, Campbell, CA, United States
        Wang, Jian-Rui, Cupertino, CA, United States
        Xue, Aidong J., Sunnyvale, CA, United States
        Xu, Chongjun, San Jose, CA, United States
        Drmanac, Radoje T., Palo Alto, CA, United States
PA      Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI      US 6436703          B1   20020820
AI      US 2000-668680           20000922 (9)
RLI     Continuation-in-part of Ser. No. US 2000-649167, filed on 23 Aug 2000
        Continuation-in-part of Ser. No. US 2000-540217, filed on 31 Mar 2000
DT      Utility
FS      GRANTED
LN.CNT 5519
INCL    INCLM: 435/325.000
        INCLS: 536/023.100; 536/023.500; 435/320.100
NCL     NCLM:  435/325.000
        NCLS:  435/320.100; 536/023.100; 536/023.500
IC      [7]
        ICM: C12N015-12
        ICS: C12N005-00
EXF     536/23.1; 536/23.5; 435/325; 435/320.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 15 OF 48  USPATFULL
AN      2002:206605  USPATFULL
TI      Novel nucleic acids and polypeptides
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IN      Tang, Y. Tom, San Jose, CA, UNITED STATES
        Zhou, Ping, Cupertino, CA, UNITED STATES
        Goodrich, Ryle, San Jose, CA, UNITED STATES
        Liu, Chenghua, San Jose, CA, UNITED STATES
        Asundi, Vinod, Foster City, CA, UNITED STATES
        Wang, Jian-Rui, Cupertino, CA, UNITED STATES
        Wang, Dunrui, Poway, CA, UNITED STATES
        Yamazaki, Victoria, Redwood Shores, CA, UNITED STATES
        Ujwal, Manusha L., Gaithersburg, MD, UNITED STATES
        Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
PI      US 2002111302      A1   20020815
AI      US 2000-728952     A1   20001130 (9)
DT      Utility
FS      APPLICATION
LN.CNT 4863
INCL    INCLM: 514/012.000
        INCLS: 530/350.000; 536/023.100; 435/069.100; 435/325.000; 435/320.100
NCL     NCLM:  514/012.000
        NCLS:  530/350.000; 536/023.100; 435/069.100; 435/325.000; 435/320.100
IC      [7]
        ICM: A61K038-17
        ICS: C07H021-04; C07K014-435; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 16 OF 48  USPATFULL
AN      2002:199275  USPATFULL
TI      Methods and compositions relating to bone-derived growth factor-like
        polypeptides
IN      Ford, John E., San Mateo, CA, UNITED STATES
PI      US 2002107386      A1   20020808
AI      US 2002-62394      A1   20020201 (10)
RLI     Continuation of Ser. No. US 1998-157305, filed on 18 Sep 1998, PENDING
DT      Utility
FS      APPLICATION
LN.CNT 3046
INCL    INCLM: 536/023.500
        INCLS: 435/006.000; 435/069.400; 435/325.000; 435/320.100; 530/399.000
NCL     NCLM:  536/023.500
        NCLS:  435/006.000; 435/069.400; 435/325.000; 435/320.100; 530/399.000
IC      [7]
        ICM: C12Q001-68
        ICS: C07H021-04; C12P021-02; C12N005-06; C07K014-51
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 17 OF 48  USPATFULL
AN      2002:191548  USPATFULL
TI      Novel Fab fragment libraries and methods for their use
IN      Hoogenboom, Hendricus Renerus Jacobus Mattheus, Maastricht, NETHERLANDS
PI      US 2002102613      A1   20020801
AI      US 2001-988899     A1   20011119 (9)
RLI     Continuation of Ser. No. WO 2000-US13682, filed on 18 May 2000, UNKNOWN
PRAI    EP 1999-201558          19990518
DT      Utility
FS      APPLICATION
LN.CNT 4310
INCL    INCLM: 435/007.100
        INCLS: 435/320.100; 530/388.100; 435/069.100; 435/326.000; 536/023.530
NCL     NCLM:  435/007.100
        NCLS:  435/320.100; 530/388.100; 435/069.100; 435/326.000; 536/023.530
IC      [7]
        ICM: G01N033-53
        ICS: C07H021-04; C12P021-02; C12N005-06; C07K016-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 18 OF 48  USPATFULL
AN      2002:191539  USPATFULL
TI      Full-length human cDNAs encoding potentially secreted proteins
IN      Milne Edwards, Jean-Baptiste Dumas, Paris, FRANCE
        Bougueleret, Lydie, Petit Lancy, SWITZERLAND
        Jobert, Severin, Paris, FRANCE
PI      US 2002102604      A1   20020801
AI      US 2000-731872     A1   20001207 (9)
PRAI    US 1999-169629P         19991208 (60)
        US 2000-187470P         20000306 (60)
DT      Utility
FS      APPLICATION
LN.CNT 28061
INCL    INCLM: 435/007.100
        INCLS: 536/023.100; 530/350.000
NCL     NCLM:  435/007.100
        NCLS:  536/023.100; 530/350.000
IC      [7]
        ICM: G01N033-53
        ICS: C07H021-02; C07H021-04; C07K001-00; C07K014-00; C07K017-00
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 19 OF 48  USPATFULL
AN      2002:188224  USPATFULL
TI      Assays involving an IL-1 receptor antagonist
IN      Ford, John, San Mateo, CA, United States
        Pace, Ann, Scotts Valley, CA, United States
PA      Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI      US 6426191         B1   20020730
AI      US 1999-457626          19991208 (9)
RLI     Continuation-in-part of Ser. No. US 1999-417455, filed on 13 Oct 1999,
        now patented, Pat. No. US 6294655 Continuation-in-part of Ser. No. US
        1999-348942, filed on 7 Jul 1999, now patented, Pat. No. US 6337072
        Continuation-in-part of Ser. No. US 1999-287210, filed on 5 Apr 1999,
        now abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on
        17 Feb 1999, now abandoned Continuation-in-part of Ser. No. US
        1998-127698, filed on 31 Jul 1998, now abandoned Continuation-in-part of
        Ser. No. US 1999-229591, filed on 13 Jan 1999, now abandoned
        Continuation of Ser. No. US 1998-99818, filed on 19 Jun 1998, now
        abandoned Continuation of Ser. No. US 127698 Continuation of Ser. No. US
        99818 Continuation-in-part of Ser. No. US 1998-82364, filed on 20 May
        1998, now abandoned Continuation-in-part of Ser. No. US 1998-79909,
        filed on 15 May 1998, now abandoned Continuation-in-part of Ser. No. US
        1998-55010, filed on 3 Apr 1998, now abandoned
DT      Utility
FS      GRANTED
LN.CNT 5305
INCL    INCLM: 435/007.800
        INCLS: 435/007.100; 435/007.200; 436/501.000; 436/502.000
NCL     NCLM:  435/007.800
        NCLS:  435/007.100; 435/007.200; 436/501.000; 436/512.000
IC      [7]
        ICM: G01N033-53
EXF     536/23.5; 530/351; 435/69.1; 435/6; 435/7.1; 435/7.2; 435/7.8; 436/501;
        436/512
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 20 OF 48  USPATFULL
AN      2002:174946  USPATFULL
TI      Chimeric polyclonal antibodies
IN      Buechler, Joe, Carlsbad, CA, United States
        Valkirs, Gunars, Escondido, CA, United States
        Gray, Jeff, Solana Beach, CA, United States
PA      Biosite Diagnostics, Inc., San Diego, CA, United States (U.S.
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        corporation)
PI      US 6420113          B1   20020716
AI      US 1999-410903           19991002 (9)
RLI     Continuation-in-part of Ser. No. WO 1998-US6704, filed on 3 Apr 1998
        Continuation-in-part of Ser. No. US 1997-835159, filed on 4 Apr 1997
        Continuation-in-part of Ser. No. US 1997-832985, filed on 4 Apr 1997,
        now patented, Pat. No. US 6057098
DT      Utility
FS      GRANTED
LN.CNT 3885
INCL    INCLM: 435/006.000
        INCLS: 435/007.100; 435/069.100; 435/320.100; 435/DIG.001; 435/DIG.002;
               435/DIG.003; 435/DIG.004; 435/DIG.014; 435/DIG.017; 536/023.100;
               536/023.530
NCL     NCLM:  435/006.000
        NCLS:  435/007.100; 435/069.100; 435/320.100; 435/DIG.001; 435/DIG.002;
               435/DIG.003; 435/DIG.004; 435/DIG.014; 435/DIG.017; 536/023.100;
               536/023.530
IC      [7]
        ICM: C12Q001-68
        ICS: C12P021-06; C07H021-02
EXF     435/6; 435/7.1; 435/7.8; 435/91.4; 435/471; 435/489; 435/69.1; 435/69.6;
        435/320.1; 435/DIG.1; 435/DIG.2; 435/DIG.3; 435/DIG.4; 435/DIG.14;
        435/DIG.17; 536/23.1; 536/23.53
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 21 OF 48  USPATFULL
AN      2002:167884  USPATFULL
TI      Antibody conjugate kits for selectively inhibiting VEGF
IN      Thorpe, Philip E., Dallas, TX, United States
        Brekken, Rolf A., Seattle, WA, United States
PA      Board of Regents, The University of Texax System, Austin, TX, United
        States (U.S. corporation)
PI      US 6416758          B1   20020709
AI      US 2000-561526           20000428 (9)
PRAI    US 1999-131432P      19990428 (60)
DT      Utility
FS      GRANTED
LN.CNT 10439
INCL    INCLM: 424/145.100
        INCLS: 424/001.490; 424/001.530; 424/001.690; 424/009.200; 424/009.300;
               424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
               424/145.100; 424/178.100; 424/179.100; 424/181.100; 424/183.100;
               424/195.110; 435/007.230; 435/069.100; 435/069.600; 435/069.700;
               435/070.210; 435/810.000; 530/387.300; 530/388.100; 530/388.150;
               530/388.240; 530/391.300; 530/391.700; 530/391.900
NCL     NCLM:  424/145.100
        NCLS:  424/001.490; 424/001.530; 424/001.690; 424/009.200; 424/009.300;
               424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
               424/178.100; 424/179.100; 424/181.100; 424/183.100; 424/195.110;
               435/007.230; 435/069.100; 435/069.600; 435/069.700; 435/070.210;
               435/810.000; 530/387.300; 530/388.100; 530/388.150; 530/388.240;
               530/391.300; 530/391.700; 530/391.900
IC      [7]
        ICM: A61K038-36
        ICS: C12P021-08; C07K016-22
EXF     424/9.2; 424/9.3; 424/133.1; 424/134.1; 424/135.1; 424/141.1; 424/142.1;
        424/145.1; 424/178.1; 424/181.1; 424/183.1; 424/195.11; 424/179.1;
        424/1.49; 424/1.53; 424/1.69; 530/387.3; 530/388.15; 530/388.24;
        530/391.3; 530/391.5; 530/391.7; 530/391.9; 435/69.6; 435/69.7;
        435/69.1; 435/70.21; 435/7.23; 435/810
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 22 OF 48  USPATFULL
AN      2002:157026  USPATFULL
TI      MEMBER OF THE IMMUNOGLOBULIN SUPERFAMILY AND USES THEREOF
IN      FORD, JOHN, SAN MATEO, CA, UNITED STATES
        YEUNG, GEORGE, SAN MATEO, CA, UNITED STATES
PI      US 2002081625       A1   20020627
AI      US 1999-417791      A1   19991014 (9)
DT      Utility
FS      APPLICATION
LN.CNT 4010
INCL    INCLM: 435/007.100
        INCLS: 536/023.530
NCL     NCLM:  435/007.100
        NCLS:  536/023.530
IC      [7]
        ICM: G01N033-53
        ICS: C07H021-04; C12P013-14; C12N005-02
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 23 OF 48  USPATFULL
AN      2002:152392  USPATFULL
TI      Methods of screening open reading frames to determine whether they
        encode polypeptides with an ability to generate an immune response
IN      Sykes, Kathryn F., Dallas, TX, United States
        Johnston, Stephen Albert, Dallas, TX, United States
PA      Board of Regents, The University of Texas System, Austin, TX, United
        States (U.S. corporation)
PI      US 6410241          B1   20020625
AI      US 2000-535366           20000324 (9)
PRAI    US 1999-125864P      19990324 (60)
        US 1999-127222P      19990331 (60)
DT      Utility
FS      GRANTED
LN.CNT 4001
INCL    INCLM: 435/006.000
        INCLS: 435/007.210
NCL     NCLM:  435/006.000
        NCLS:  435/007.210
IC      [7]
        ICM: C12Q001-68
EXF     435/6; 435/7.1; 435/325; 435/7.21; 514/44
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 24 OF 48  USPATFULL
AN      2002:143940  USPATFULL
TI      Cancer treatment methods using antibodies to aminophospholipids
IN      Thorpe, Philip E., Dallas, TX, United States
        Ran, Sophia, Dallas, TX, United States
PA      Board of Regents, The University of Texas System, Austin, TX, United
        States (U.S. corporation)
PI      US 6406693          B1   20020618
AI      US 1999-351543           19990712 (9)
PRAI    US 1998-110608P      19981202 (60)
        US 1998-92672P       19980713 (60)
DT      Utility
FS      GRANTED
LN.CNT 7541
INCL    INCLM: 424/130.100
        INCLS: 424/132.100; 424/133.100; 424/135.100; 424/138.100; 424/141.100;
               424/152.100; 424/184.100; 530/387.100; 435/006.000
NCL     NCLM:  424/130.100
        NCLS:  424/132.100; 424/133.100; 424/135.100; 424/138.100; 424/141.100;
               424/152.100; 424/184.100; 435/006.000; 530/387.100
IC      [7]
        ICM: A61K039-395
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     ICS: C07K016-00; C07K016-28; C07K016-30; C12Q001-68
EXF    424/130.1; 424/184.1; 424/132.1; 424/133.1; 424/135.1; 424/138.1;
       424/141.1; 424/152.1; 530/387.1; 435/6
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 25 OF 48  USPATFULL
AN     2002:119584  USPATFULL
TI     Novel nucleic acids and polypeptides
IN     Tang, Y. Tom, San Jose, CA, UNITED STATES
       Liu, Chenghua, San Jose, CA, UNITED STATES
       Zhou, Ping, Cupertino, CA, UNITED STATES
       Asundi, Vinod, Foster City, CA, UNITED STATES
       Ren, Feiyan, Cupertino, CA, UNITED STATES
       Zhang, Jie, Campbell, CA, UNITED STATES
       Zhao, Qing A., San Jose, CA, UNITED STATES
       Xue, Aidong J., Sunnyvale, CA, UNITED STATES
       Goodrich, Ryle, San Jose, CA, UNITED STATES
       Wehrman, Tom, Stanford, CA, UNITED STATES
       Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
PI     US 2002061567      A1   20020523
AI     US 2000-728711     A1   20001130 (9)
RLI    Continuation-in-part of Ser. No. US 2000-649167, filed on 23 Aug 2000,
       PENDING Continuation-in-part of Ser. No. US 2000-540217, filed on 31 Mar
       2000, PENDING
DT     Utility
FS     APPLICATION
LN.CNT 5921
INCL   INCLM: 435/183.000
       INCLS: 435/069.100; 435/325.000; 435/320.100; 536/023.200
NCL    NCLM:  435/183.000
       NCLS:  435/069.100; 435/325.000; 435/320.100; 536/023.200
IC     [7]
       ICM: C12N009-00
       ICS: C07H021-04; C12P021-02; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 26 OF 48  USPATFULL
AN     2002:116388  USPATFULL
TI     Antibodies specific for EGF motif proteins
IN     Ford, John, 2763 S. Norfolk, #210, San Mateo, CA, United States  94403
       Yeung, George, 102 Magnolia La., Mountainview, CA, United States  94043
PI     US 6392019         B1   20020521
AI     US 1999-363316          19990728 (9)
RLI    Continuation-in-part of Ser. No. US 1999-249697, filed on 12 Feb 1999
       Continuation-in-part of Ser. No. US 1997-968800, filed on 22 Nov 1997,
       now abandoned
DT     Utility
FS     GRANTED
LN.CNT 3505
INCL   INCLM: 530/387.900
       INCLS: 530/300.000; 530/350.000; 530/387.100; 530/388.100; 530/389.100
NCL    NCLM:  530/387.900
       NCLS:  530/300.000; 530/350.000; 530/387.100; 530/388.100; 530/389.100
IC     [7]
       ICM: C07K002-00
       ICS: C07K014-00; C07K016-00; C07K016-18
EXF    435/331; 530/387.1; 530/387.9; 530/388.1; 530/388.15; 530/389.1;
       530/391.3; 530/300; 530/35D; 530/388.23; 530/388.24; 530/389.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 27 OF 48  USPATFULL
AN     2002:116387  USPATFULL
TI     EGF MOTIF protein obtained from a cDNA library of fetal liver-spleen
IN     Ford, John, San Mateo, CA, United States
       Yeung, George, Mountainview, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6392018         B1   20020521
AI     US 1999-249697          19990212 (9)
RLI    Continuation-in-part of Ser. No. US 1997-968800, filed on 22 Nov 1997,
       now abandoned
DT     Utility
FS     GRANTED
LN.CNT 3353
INCL   INCLM: 530/351.000
       INCLS: 530/350.000; 530/324.000; 530/326.000; 514/002.000; 424/085.100
NCL    NCLM:  530/351.000
       NCLS:  424/085.100; 530/324.000; 530/326.000; 530/350.000
IC     [7]
       ICM: C07K017-00
       ICS: C07K007-04; A61K045-00; A61K038-00
EXF    530/350; 530/300; 530/324; 530/351; 530/326; 530/327; 435/69.1;
       435/320.1; 435/325; 435/252.3; 435/7.1; 424/130.1; 420/130.1; 536/23.5
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 28 OF 48  USPATFULL
AN     2002:112286  USPATFULL
TI     Novel interleukin-3 and uses thereof
IN     Ford, John, San Mateo, CA, UNITED STATES
PA     Hyseq, Inc. (U.S. corporation)
PI     US 2002058018      A1   20020516
AI     US 2001-792246     A1   20010223 (9)
RLI    Continuation of Ser. No. US 1999-376732, filed on 17 Aug 1999, UNKNOWN
DT     Utility
FS     APPLICATION
LN.CNT 5626
INCL   INCLM: 424/085.200
       INCLS: 435/069.520; 435/325.000; 435/007.100; 536/023.500; 530/351.000
NCL    NCLM:  424/085.200
       NCLS:  435/069.520; 435/325.000; 435/007.100; 536/023.500; 530/351.000
IC     [7]
       ICM: A61K038-20
       ICS: G01N033-53; C07H021-04; C12N005-06; C07K014-54
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 29 OF 48  USPATFULL
AN     2002:108835  USPATFULL
TI     Methods and materials relating to novel CD39-like polypeptides
IN     Ford, John, San Mateo, CA, United States
       Mulero, Julio J., Palo Alto, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6387645         B1   20020514
AI     US 1999-350836          19990709 (9)
RLI    Continuation-in-part of Ser. No. US 1999-273447, filed on 19 Mar 1999,
       now abandoned Continuation-in-part of Ser. No. US 1998-122449, filed on
       24 Jul 1998, now abandoned Continuation-in-part of Ser. No. US
       1998-118205, filed on 16 Jul 1998, now abandoned
DT     Utility
FS     GRANTED
LN.CNT 2423
INCL   INCLM: 435/021.000
       INCLS: 435/018.000
NCL    NCLM:  435/021.000
       NCLS:  435/018.000
IC     [7]
       ICM: C12Q001-42
EXF    435/7.1; 435/18; 435/21
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L13  ANSWER 30 OF 48  USPATFULL
AN     2002:81614  USPATFULL
TI     Interleukin--1 Hy2 materials and methods
IN     Ballinger, Dennis G., Menlo Park, CA, United States
       Pace, Ann M., Scotts Valley, CA, United States
       Lin, Hai Shan, Castro Valley, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6372892          B1    20020416
AI     US 2000-522964            20000310 (9)
RLI    Continuation-in-part of Ser. No. US 1999-316086, filed on 20 May 1999,
       now patented, Pat. No. US 6175532
DT     Utility
FS     GRANTED
LN.CNT 4690
INCL   INCLM: 530/389.200
       INCLS: 350/351.000
NCL    NCLM:  530/389.200
       NCLS:  530/350.000; 530/351.000
IC     [7]
       ICM: C07K017-00
       ICS: C07K016-00
EXF    530/351; 530/389.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 31 OF 48  USPATFULL
AN     2002:78408  USPATFULL
TI     Prostate cancer-related compositions, methods, and kits based on DNA
       macroarray proteomics platforms
IN     Stearns, Mark, Villanova, PA, UNITED STATES
       Hu, Youji, Gulph Mills, PA, UNITED STATES
       Wang, Min, Gulph Mills, PA, UNITED STATES
PI     US 2002042062       A1    20020411
AI     US 2001-813380      A1    20010321 (9)
RLI    Continuation-in-part of Ser. No. WO 2000-US25981, filed on 24 Sep 2000,
       UNKNOWN
PRAI   US 1999-155865P       19990924 (60)
DT     Utility
FS     APPLICATION
LN.CNT 6916
INCL   INCLM: 435/006.000
       INCLS: 435/007.230; 435/325.000; 435/069.300; 536/023.500; 530/350.000;
              435/183.000
NCL    NCLM:  435/006.000
       NCLS:  435/007.230; 435/325.000; 435/069.300; 536/023.500; 530/350.000;
              435/183.000
IC     [7]
       ICM: C12Q001-68
       ICS: G01N033-574; C07H021-04; C12N009-00; C12P021-02; C12N005-06;
       C07K014-47
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 32 OF 48  USPATFULL
AN     2002:70108  USPATFULL
TI     Polynucleotides encoding IL-1 Hy2 polypeptides
IN     Ballinger, Dennis G., Menlo, CA, United States
       Ford, John, San Mateo, CA, United States
       Ho, Alice Suk-Yue, Union City, CA, United States
       Lin, Hai Shan, Castro Valley, CA, United States
       Pace, Ann M., Scotts Valley, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6365726          B1    20020402
AI     US 2000-578458            20000522 (9)
RLI    Continuation-in-part of Ser. No. US 2000-522964, filed on 10 Mar 2000
       Continuation-in-part of Ser. No. US 1999-316081, filed on 20 May 1999,
       now patented, Pat. No. US 6339141
DT     Utility
FS     GRANTED
LN.CNT 4803
INCL   INCLM: 536/023.520
       INCLS: 536/023.100; 536/023.500; 536/024.310; 435/069.100; 435/069.520;
              435/320.100
NCL    NCLM:  536/023.520
       NCLS:  435/069.100; 435/069.520; 435/320.100; 536/023.100; 536/023.500;
              536/024.310
IC     [7]
       ICM: C07H021-04
       ICS: C12P021-06; C12N015-00; C12N015-06
EXF    435/69.1; 435/69.52; 435/320.1; 435/23.1; 536/23.5; 536/23.52;
       536/24.31; 530/350; 530/357
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 33 OF 48  USPATFULL
AN     2002:67174  USPATFULL
TI     Novel matrix metalloproteinase (MMP-25) expressed in skin cells
IN     Wang, Kai, Bellevue, WA, UNITED STATES
       Smith, Ryan, Seattle, WA, UNITED STATES
       Fajardo, Mark, Shoreline, WA, UNITED STATES
       Moss, Patrick, Shoreline, WA, UNITED STATES
       Schatzman, Randall C., Shoreline, WA, UNITED STATES  LR
PI     US 2002037827       A1    20020328
AI     US 2001-801196      A1    20010306 (9)
PRAI   US 2000-187196P       20000306 (60)
DT     Utility
FS     APPLICATION
LN.CNT 4015
INCL   INCLM: 514/001.000
       INCLS: 435/226.000; 800/008.000; 435/325.000; 435/069.100; 536/023.200
NCL    NCLM:  514/001.000
       NCLS:  435/226.000; 800/008.000; 435/325.000; 435/069.100; 536/023.200
IC     [7]
       ICM: A61K031-00
       ICS: A01K067-00; C07H021-04; C12N009-64; C12N005-06; C12P021-02
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 34 OF 48  USPATFULL
AN     2002:39654  USPATFULL
TI     Methods and compositions relating to CD39-like polypeptides and nucleic
       acids
IN     Chadwick, Brian Paul, Allston, MA, United States
       Frischauf, Anna-Maria, London, UNITED KINGDOM
PA     HYSEQ, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6350447          B1    20020226
AI     US 1999-240639            19990129 (9)
DT     Utility
FS     GRANTED
LN.CNT 4954
INCL   INCLM: 424/094.600
       INCLS: 435/195.000; 514/012.000; 530/350.000
NCL    NCLM:  424/094.600
       NCLS:  435/195.000; 514/012.000; 530/350.000
IC     [7]
       ICM: A61K038-46
       ICS: C12N009-14; C07K014-435
EXF    435/195; 514/12; 424/94.6; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 35 OF 48  USPATFULL
AN     2002:19060  USPATFULL
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TI     Antibody conjugate compositions for selectively inhibiting VEGF
IN     Thorpe, Philip E., Dallas, TX, United States
       Brekken, Rolf A., Seattle, WA, United States
PA     Board of Regents, The University of Texas System, Austin, TX, United
       States (U.S. corporation)
PI     US 6342221          B1    20020129
AI     US 2000-561108            20000428 (9)
PRAI   US 1999-131432P       19990428 (60)
DT     Utility
FS     GRANTED
LN.CNT 10492
INCL   INCLM: 424/178.100
       INCLS: 424/130.100; 424/179.100; 424/181.100; 424/183.100; 424/193.100;
              424/195.110; 424/001.490; 424/001.530; 424/009.300; 424/009.340;
              424/009.600; 435/007.210; 435/069.100; 435/070.210; 435/810.000;
              435/007.230; 435/007.100; 530/391.100; 530/391.300; 530/391.500;
              530/391.700; 530/391.900
NCL    NCLM:  424/178.100
       NCLS:  424/001.490; 424/001.530; 424/009.300; 424/009.340; 424/009.600;
              424/130.100; 424/179.100; 424/181.100; 424/183.100; 424/193.100;
              424/195.110; 435/007.100; 435/007.210; 435/007.230; 435/069.100;
              435/070.210; 435/810.000; 530/391.100; 530/391.300; 530/391.500;
              530/391.700; 530/391.900
IC     [7]
       ICM: A61K039-44
       ICS: A61K039-395
EXF    424/130.1; 424/133.1; 424/134.1; 424/135.1; 424/141.1; 424/142.1;
       424/143.1; 424/178.1; 424/181.1; 424/183.1; 424/195.11; 424/179.1;
       424/1.49; 424/1.53; 424/1.69; 424/193.1; 424/9.3; 424/9.34; 424/9.6;
       530/387.1; 530/387.3; 530/388.1; 530/388.15; 530/388.22; 530/391.1;
       530/391.3; 530/391.5; 530/391.7; 530/391.9; 530/809; 530/864; 530/865;
       530/866; 435/7.1; 435/69.1; 435/70.21; 435/810; 435/7.21; 435/7.23
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 36 OF 48  USPATFULL
AN     2002:19058  USPATFULL
TI     Antibody compositions for selectively inhibiting VEGF
IN     Thorpe, Philip E., Dallas, TX, United States
       Brekken, Rolf A., Seattle, WA, United States
PA     Board of Regents, The University of Texas System, Austin, TX, United
       States (U.S. corporation)
PI     US 6342219          B1    20020129
AI     US 2000-561500            20000428 (9)
PRAI   US 1999-131432P       19990428 (60)
DT     Utility
FS     GRANTED
LN.CNT 10403
INCL   INCLM: 424/145.100
       INCLS: 424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
              424/143.100; 435/069.100; 435/335.000; 435/810.000; 530/387.100;
              530/387.300; 530/388.100; 530/388.150; 530/388.230; 530/391.100;
              530/391.300; 530/391.500; 530/391.700; 530/809.000; 530/864.000;
              530/865.000; 530/866.000
NCL    NCLM:  424/145.100
       NCLS:  424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
              424/143.100; 435/069.100; 435/335.000; 435/810.000; 530/387.100;
              530/387.300; 530/388.100; 530/388.150; 530/388.230; 530/391.100;
              530/391.300; 530/391.500; 530/391.700; 530/809.000; 530/864.000;
              530/865.000; 530/866.000
IC     [7]
       ICM: A61K039-395
       ICS: C12P021-08; C07K016-00
EXF    424/130.1; 424/133.1; 424/134.1; 424/135.1; 424/141.1; 424/142.1;
       424/143.1; 424/145.1; 435/810; 435/69.1; 435/335; 530/387.1; 530/387.3;
       530/388.1; 530/388.15; 530/388.23; 530/391.1; 530/391.3; 530/391.5;
       530/391.7; 530/809; 530/864; 530/865; 530/866
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 37 OF 48  USPATFULL
AN     2002:16906  USPATFULL
TI     Novel nucleic acids and polypeptides
IN     Tang, Y. Tom, San Jose, CA, UNITED STATES
       Zhou, Ping, Cupertino, CA, UNITED STATES
       Goodrich, Ryle, San Jose, CA, UNITED STATES
       Liu, Chenghua, San Jose, CA, UNITED STATES
       Asundi, Vinod, Foster City, CA, UNITED STATES
       Xue, Aidong J., Sunnyvale, CA, UNITED STATES
       Zhang, Jie, Campbell, CA, UNITED STATES
       Zhao, Qing A., San Jose, CA, UNITED STATES
       Ren, Feiyan, Cupertino, CA, UNITED STATES
       Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
PI     US 2002009786       A1    20020124
AI     US 2000-728628      A1    20001201 (9)
RLI    Continuation-in-part of Ser. No. US 2000-552929, filed on 18 Apr 2000,
       UNKNOWN
DT     Utility
FS     APPLICATION
LN.CNT 5748
INCL   INCLM: 435/183.000
       INCLS: 435/069.100; 435/325.000; 536/023.200
NCL    NCLM:  435/183.000
       NCLS:  435/069.100; 435/325.000; 536/023.200
IC     [7]
       ICM: C12P021-02
       ICS: C07H021-04; C12N009-00; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 38 OF 48  USPATFULL
AN     2002:9923  USPATFULL
TI     Interleukin-1 Hy2 materials and methods
IN     Ballinger, Dennis G., Menlo Park, CA, United States
       Pace, Ann M., Scots Valley, CA, United States
PA     Hycey Inc., Sunnydale, CA, United States (U.S. corporation)
PI     US 6339141          B1    20020115
AI     US 1999-316081            19990520 (9)
DT     Utility
FS     GRANTED
LN.CNT 4019
INCL   INCLM: 530/351.000
       INCLS: 424/085.200; 424/143.100; 424/145.100
NCL    NCLM:  530/351.000
       NCLS:  424/085.200; 424/143.100; 424/145.100
IC     [7]
       ICM: C07K017-00
       ICS: A61K045-00; A61K039-395
EXF    530/357; 424/85.2; 424/143.1; 424/145.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 39 OF 48  USPATFULL
AN     2002:5759  USPATFULL
TI     Interleukin-1 receptor antagonist and recombinant production thereof
IN     Ford, John, San Mateo, CA, United States
       Pace, Ann, Scotts Valley, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6337072          B1    20020108
AI     US 1999-348942            19990707 (9)
RLI    Continuation-in-part of Ser. No. US 1999-287210, filed on 5 Apr 1999,
       now abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on
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       17 Feb 1999, now abandoned Continuation-in-part of Ser. No. US
       1999-229591, filed on 13 Jan 1999, now abandoned Continuation-in-part of
       Ser. No. US 1998-127698, filed on 31 Jul 1998, now abandoned
       Continuation of Ser. No. US 1998-99818, filed on 19 Jun 1998, now
       abandoned Continuation of Ser. No. US 1998-82364, filed on 20 May 1998,
       now abandoned Continuation-in-part of Ser. No. US 1998-79909, filed on
       15 May 1998, now abandoned Continuation-in-part of Ser. No. US
       1998-55010, filed on 3 Apr 1998, now abandoned
PRAI   WO 1999-US4291       19990405
DT     Utility
FS     GRANTED
LN.CNT 5025
INCL   INCLM: 424/198.100
       INCLS: 536/023.500; 435/069.100; 435/069.520; 435/325.000; 435/252.300;
              435/320.100; 514/002.000; 530/350.000; 530/351.000; 530/402.000;
              424/001.690
NCL    NCLM:  424/198.100
       NCLS:  424/001.690; 435/069.100; 435/069.520; 435/252.300; 435/320.100;
              435/325.000; 514/002.000; 530/350.000; 530/351.000; 530/402.000;
              536/023.500
IC     [7]
       ICM: C07K014-54
       ICS: C07K021-04; A61K038-20
EXF    530/350; 530/351; 435/69.1; 435/69.5; 435/69.52; 435/325; 435/252.3;
       435/320.1; 536/23.5; 514/2; 424/198.1; 424/1.69
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 40 OF 48  USPATFULL
AN     2002:926  USPATFULL
TI     Methods and materials relating to CD39-like polypeptides
IN     Ford, John, San Mateo, CA, United States
       Mulero, Julio J., Palo Alto, CA, United States
       Yeung, George, Mountain View, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6335013          B1    20020101
AI     US 2000-608285           20000630 (9)
RLI    Continuation-in-part of Ser. No. US 2000-583231, filed on 26 May 2000
       Continuation-in-part of Ser. No. US 2000-557800, filed on 25 Apr 2000
       Continuation-in-part of Ser. No. US 2000-481238, filed on 11 Jan 2000
       Continuation-in-part of Ser. No. US 1999-370265, filed on 9 Aug 1999
       Continuation-in-part of Ser. No. WO 1999-US16180, filed on 16 Jul 1999
       Continuation-in-part of Ser. No. US 1999-350836, filed on 9 Jul 1999
       Continuation-in-part of Ser. No. US 1999-273447, filed on 19 Mar 1999
DT     Utility
FS     GRANTED
LN.CNT 4738
INCL   INCLM: 424/094.610
       INCLS: 514/012.000
NCL    NCLM:  424/094.610
       NCLS:  514/012.000
IC     [7]
       ICM: A61K038-47
EXF    435/13; 435/18; 424/94.61; 514/12
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 41 OF 48  USPATFULL
AN     2001:196603  USPATFULL
TI     Cancer treatment methods using therapeutic conjugates that bind to
       aminophospholipids
IN     Thorpe, Philip E., Dallas, TX, United States
       Ran, Sophia, Dallas, TX, United States
PA     Board of Regents, The University of Texas System, Austin, TX, United
       States (U.S. corporation)
PI     US 6312694          B1    20011106
AI     US 1999-351457           19990712 (9)
PRAI   US 1998-92589P       19980713 (60)
       US 1998-110600P      19981202 (60)
DT     Utility
FS     GRANTED
LN.CNT 8243
INCL   INCLM: 424/178.100
       INCLS: 424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100;
              424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100;
              514/012.000; 530/387.100; 530/388.100
NCL    NCLM:  424/178.100
       NCLS:  424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100;
              424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100;
              514/012.000; 530/387.100; 530/388.100
IC     [7]
       ICM: A61K039-395
       ICS: C12P021-08; C07K016-00
EXF    514/12; 424/133.1; 424/135.1; 424/136.1; 424/137.1; 424/141.1;
       424/142.1; 424/143.1; 424/178.1; 424/181.1; 424/193.1; 530/387.1;
       530/388.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 42 OF 48  USPATFULL
AN     2001:178817  USPATFULL
TI     Method for generating libraries of antibody genes comprising
       amplification of diverse antibody DNAs and methods for using these
       libraries for the production of diverse antigen combining molecules
IN     Wigler, Michael H., Lloyd Harbor, NY, United States
       Sorge, Joseph A., Rancho Santa Fe, CA, United States
PA     Stratagene, San Diego, CA, United States (U.S. corporation)
PI     US 6303313          B1    20011016
AI     US 1999-439732           19991112 (9)
RLI    Continuation of Ser. No. US 1997-997195, filed on 23 Dec 1997
       Continuation of Ser. No. US 1994-315269, filed on 29 Sep 1994, now
       patented, Pat. No. US 5780225 Continuation of Ser. No. US 1992-919730,
       filed on 24 Jul 1992, now patented, Pat. No. US 5284555 Continuation of
       Ser. No. US 1990-464350, filed on 11 Jan 1990, now abandoned
PRAI   WO 1991-US209        19910110
DT     Utility
FS     GRANTED
LN.CNT 1039
INCL   INCLM: 435/006.000
       INCLS: 435/091.200
NCL    NCLM:  435/006.000
       NCLS:  435/091.200
IC     [7]
       ICM: C12Q001-68
       ICS: C12P019-34
EXF    435/6; 435/91.2; 536/22.1; 536/23.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 43 OF 48  USPATFULL
AN     2001:163325  USPATFULL
TI     Nucleic acids encoding B7-1 and B7-2 molecules
IN     Sharpe, Arlene H., Brookline, MA, United States
       Borriello, Francescopaolo, Brookline, MA, United States
       Freeman, Gordon J., Brookline, MA, United States
       Nadler, Lee M., Newton, MA, United States
PA     Dana-Farber Cancer Institute Brigham, Boston, MA, United States (U.S.
       corporation)
       Women's Hospital, Boston, MA, United States (U.S. corporation)
PI     US 6294660          B1    20010925
       WO 9523859  19950908
AI     US 1997-702525           19970207 (8)
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       WO 1995-US2576          19950302
                               19970207  PCT 371 date
                               19970207  PCT 102(e) date
RLI    Continuation-in-part of Ser. No. US 1994-205697, filed on 2 Mar 1994,
       now patented, Pat. No. US 6218510
DT     Utility
FS     GRANTED
LN.CNT 2271
INCL   INCLM: 536/023.500
       INCLS: 536/023.100; 530/350.000
NCL    NCLM:  536/023.500
       NCLS:  530/350.000; 536/023.100
IC     [7]
       ICM: C12N015-12
       ICS: C12N015-11; C07K014-705
EXF    435/69.1; 435/70.1; 435/71.1; 435/172.2; 435/172.03; 435/243; 435/252.3;
       435/320.1; 435/440; 435/455; 530/350; 536/23.1; 536/23.4; 536/23.5
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 44 OF 48  USPATFULL
AN     2001:163320  USPATFULL
TI     Anti-interleukin-1 receptor antagonist antibodies and uses thereof
IN     Ford, John, San Mateo, CA, United States
       Pace, Ann, Scotts Valley, CA, United States
PA     Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI     US 6294655         B1    20010925
AI     US 1999-417455           19991013 (9)
RLI    Continuation-in-part of Ser. No. US 1999-348942, filed on 7 Jul 1999
       Continuation of Ser. No. US 1999-287210, filed on 5 Apr 1999, now
       abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on 17
       Feb 1999, now abandoned Continuation-in-part of Ser. No. US 1998-127698,
       filed on 31 Jul 1998, now abandoned Continuation-in-part of Ser. No. US
       1999-229591, filed on 13 Jan 1999, now abandoned Continuation of Ser.
       No. US 1998-99818, filed on 19 Jun 1998, now abandoned , said Ser. No.
       US 127698 Continuation-in-part of Ser. No. US 1998-82364, filed on 20
       May 1998, now abandoned , said Ser. No. US 99818 Continuation-in-part of
       Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned
       Continuation-in-part of Ser. No. US 1998-79909, filed on 15 May 1998,
       now abandoned Continuation-in-part of Ser. No. US 1998-55010, filed on 3
       Apr 1998, now abandoned
DT     Utility
FS     GRANTED
LN.CNT 4656
INCL   INCLM: 530/388.230
       INCLS: 530/387.900; 530/388.100; 530/388.150; 530/389.100; 530/391.100;
              530/391.300; 530/350.000; 536/023.500; 436/501.000; 435/007.100;
              424/134.100; 424/139.100; 424/141.100; 424/145.100
NCL    NCLM:  530/388.230
       NCLS:  424/134.100; 424/139.100; 424/141.100; 424/145.100; 435/007.100;
              436/501.000; 530/350.000; 530/387.900; 530/388.100; 530/388.150;
              530/389.100; 530/391.100; 530/391.300; 536/023.500
IC     [7]
       ICM: C07K016-18
       ICS: C12P021-08
EXF    435/69.1; 435/69.7; 435/7.1; 536/23.5; 536/23.53; 436/501; 424/134.1;
       424/139.1; 424/141.1; 424/145.1; 530/387.9; 530/388.1; 530/388.15;
       530/388.23; 530/389.1; 530/391.1; 530/391.3; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 45 OF 48  USPATFULL
AN     2000:171124  USPATFULL
TI     Metal-regulated transporters and uses therefor
IN     Guerinot, Mary Lou, Etna, NH, United States
       Eide, David J., Columbia, MO, United States
PA     Trustees of Dartmouth College, Hanover, NH, United States (U.S.
       corporation)
       Regents of the University of Minnesota, Minneapolis, MN, United States
       (U.S. corporation)
PI     US 6162900               20001219
AI     US 1998-107858           19980630 (9)
RLI    Division of Ser. No. US 1996-758621, filed on 27 Nov 1996, now patented,
       Pat. No. US 5846821
PRAI   CA 1996-2187728      19961011
       US 1996-18578P       19960529 (60)
DT     Utility
FS     Granted
LN.CNT 4260
INCL   INCLM: 530/370.000
       INCLS: 435/419.000; 435/070.100; 435/071.100; 435/252.300
NCL    NCLM:  530/370.000
       NCLS:  435/070.100; 435/071.100; 435/252.300; 435/419.000
IC     [7]
       ICM: C12N015-00
EXF    800/278; 800/298; 435/320.1; 435/6; 435/69.1; 435/172.3; 435/325;
       435/410; 435/419; 435/70.1; 435/71.1; 435/252.3; 530/350; 530/370;
       530/377; 530/300; 530/324; 530/325; 530/326; 530/327; 530/328; 536/23.6;
       424/278.1; 424/617; 424/639; 424/641; 424/646; 424/654; 514/44
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 46 OF 48  USPATFULL
AN     2000:50562  USPATFULL
TI     Receptor-mediated gene delivery using bacteriophage vectors
IN     Larocca, David, Encinitas, CA, United States
       Baird, Andrew, San Diego, CA, United States
       Johnson, Wendy, Encinitas, CA, United States
PA     Selective Genetics, Inc., San Diego, CA, United States (U.S.
       corporation)
PI     US 6054312               20000425
AI     US 1997-920396           19970829 (8)
DT     Utility
FS     Granted
LN.CNT 2350
INCL   INCLM: 435/320.100
       INCLS: 530/350.000; 530/387.100; 536/023.500; 536/023.720
NCL    NCLM:  435/320.100
       NCLS:  530/350.000; 530/387.100; 536/023.500; 536/023.720
IC     [7]
       ICM: C12N015-63
       ICS: C12N015-33; C12N015-12; C07K014-00
EXF    514/44; 435/320.1; 530/350; 530/387.1; 536/24.5; 536/23.5; 536/23.72
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 47 OF 48  USPATFULL
AN     1998:154133  USPATFULL
TI     Metal-regulated transporters and uses therefor
IN     Guerinot, Mary Lou, Etna, NH, United States
       Eide, David J., Columbia, MS, United States
PA     Trustees of Dartmouth College, Hanover, NH, United States (U.S.
       corporation)
       Regents of the University of Minnesota, Minneapolis, MN, United States
       (U.S. corporation)
PI     US 5846821               19981208
AI     US 1996-758621           19961127 (8)
PRAI   US 1996-18578P       19960529 (60)
DT     Utility
FS     Granted
LN.CNT 4077
INCL   INCLM: 435/320.100
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       INCLS: 435/006.000; 435/069.100; 435/172.300; 435/325.000; 436/501.000;
              536/023.100; 536/024.100; 536/024.300; 536/024.310; 536/024.320;
              536/024.330; 935/077.000; 935/078.000
NCL    NCLM:  435/320.100
       NCLS:  435/006.000; 435/069.100; 435/325.000; 436/501.000; 536/023.100;
              536/024.100; 536/024.300; 536/024.310; 536/024.320; 536/024.330
IC     [6]
       ICM: C07H021-04
EXF    435/6; 435/69.1; 435/172.3; 435/320.1; 435/325; 436/501; 536/23.1;
       536/24.1; 536/24.3-24.33; 935/77; 935/78
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13  ANSWER 48 OF 48  USPATFULL
AN     1998:82528  USPATFULL
TI     Method for generating libaries of antibody genes comprising
       amplification of diverse antibody DNAs and methods for using these
       libraries for the production of diverse antigen combining molecules
IN     Wigler, Michael H., Lloyd Harbor, NY, United States
       Sorge, Joseph A., Rancho Santa Fe, CA, United States
PA     Stratagene, La Jolla, CA, United States (U.S. corporation)
PI     US 5780225              19980714
AI     US 1994-315269          19940929 (8)
RLI    Continuation of Ser. No. US 1992-919370, filed on 23 Jul 1992 which is a
       continuation of Ser. No. US 1990-464530, filed on 11 Jan 1990
DT     Utility
FS     Granted
LN.CNT 1174
INCL   INCLM: 435/006.000
       INCLS: 435/069.100
NCL    NCLM:  435/006.000
       NCLS:  435/069.100
IC     [6]
       ICM: C12Q001-68
       ICS: C12P021-00
EXF    435/5; 435/6; 435/91.2; 435/69.1; 435/69.7
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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odies. In: Catalytic antibodies. Wiley,
173
ıe analogy. Comparison of enzymes and
yrosine. Biochemistry 14:591-599
M, Schreiber SL 1990 Inhibition of FKBP
ᶠK506: twisted amide surrogate. Science

Construction of combinatorial antibody expression libraries in *Escherichia coli*

W. Huse

Ixsys Inc, 3550 General Atomics Court, Suite L103, San Diego, CA 92121, USA

Abstract. A λ vector system has been developed for the construction and coexpression of diverse populations of heavy and light chain cDNA sequences. Heavy and light chain sequences within the immunological repertoire are generated by the polymerase chain reaction using primers directed to conserved regions within the variable region framework. Two λ vectors are employed for the independent construction of heavy and light chain cDNA libraries. The libraries are randomly combined to produce a population of λ phage with each containing one heavy and one light chain cDNA sequence. The vectors direct the synthesis and secretion of functional Fab antibody fragments from a dicistronic operon. Libraries of up to 1×10^7 recombinants can be obtained with a diversity approaching *in vivo* estimates. Analysis of the heavy and light chain combinations reveals that the complete antibody repertoire can be generated by subsequent reshuffling of heavy and light chain cDNAs within an initial Fab-producing library. Inherent bias found *in vivo* toward certain heavy and light chain combinations can be virtually eliminated.

1991 Catalytic antibodies. Wiley, Chichester (Ciba Foundation Symposium 159) p 91–102

Monoclonal antibodies have been generated that catalyse a broad range of chemical transformations (Shokat et al 1989, Iverson & Lerner 1989). The rationale is to immunize mice with predicted transition state analogues in the hope that antibodies which bind the analogues specifically will function analogously to known enzymic mechanisms when presented with substrate. Apart from the unpredictable design of appropriate transition state analogues, the probability of finding antibodies where particular amino acid side chains participate in catalysis also depends on the number of different antibodies assayed.

Current methods for generating monoclonal antibodies do not provide an adequate survey of the natural immunological repertoire. For example, in an individual animal there are at least 5–10 000 different B cell clones capable of generating unique antibodies to a relatively small antigen (Schreier 1978, Lawrence et al 1973, Chiller & Weigle 1970). The *in vivo* process of somatic

mutation during the generation of antibody diversity additionally generates essentially an unlimited number of unique antibodies. In contrast, owing to the relative inefficiency of the *in vitro* process, the production of monoclonal antibodies generally results in only a few hundred different antibodies.

Successful expression of recombinant antibody molecules in bacterial systems has recently been accomplished (Skerra & Plückthun 1988, Better et al 1988). These prokaryotic systems satisfy all the criteria for assembly of functional antibody fragments. First, synthesis of approximately stoichiometric amounts of heavy and light chains can be accomplished by expressing both chains under the control of a single promoter. Second, transport of both precursor proteins to the periplasmic space occurs efficiently and accurately with correct processing of signal sequences. Third, recombinant antibody fragments are correctly folded into functional domains with correct disulphide bond formation. Fourth, heavy and light chain antibody fragments are self-assembled into functional heterodimers. Additionally, libraries have been constructed which express diverse populations of only heavy (V_H) chain polypeptides (Sastry et al 1989, Ward et al 1989). The antigen-binding affinity of single heavy chains for use as substitutes of Fab fragments is, however, one to two orders of magnitude lower than that of heterodimers. More importantly, heavy chains lose specificity because they tend to be sticky (Ward et al 1989).

The expression of antibody fragment libraries is an important extension of the recombinant expression of unique antibody species. Polymerase chain reaction (PCR) technology has allowed access to the diverse family of antibody genes via conserved sequences in the 5′ and 3′ portions of the variable, the framework and the constant region sequences. Specific amplification of antibody fragments using primers homologous to these conserved sequences allows the construction of libraries containing large populations of heavy and light chain antibody fragments. We report the use of λ phage libraries to generate diverse populations of functional Fab fragments. The system parallels the natural immunological repertoire, and reduces the inherent bias towards a small number of predominant species that is found within an *in vivo* population. Libraries can be constructed and screened for a desired antigen-binding activity in less than two weeks. This efficiency allows the rapid isolation of rare catalytic antibodies in a form suitable for genetic manipulation.

Results and discussion

To obtain a vector system for generating a large number of Fab fragments that could be screened directly, we constructed the expression libraries in modified bacteriophage λ expression vectors. Coexpression libraries are made by first producing separate heavy (V_H) and light (V_L) chain fragment libraries, then randomly combining the two libraries into a single vector population (Huse et al 1989). Each Fab fragment coexpressed from a single vector within the

dy diversity additionally generates
ıntibodies. In contrast, owing to the
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randomly combined population retains all the characteristics exhibited by recombinant antibody fragments expressed singly. Moreover, random combination of both chains serves as a source of diversity and increases the total number of sequences which can be obtained.

The vectors used for expression of V_H and V_L sequences have been previously reported (Huse et al 1989) and are schematically represented in Fig. 1. Populations of V_L sequences are cloned into the λ light chain vector; V_H sequences are cloned into the λ heavy chain vector. The vectors are designed to be asymmetric with respect to the *Not*I and *Eco*RI restriction sites which flank the cloning and expression sequences. The asymmetric placement of these restriction sites in a linear vector allows the V_L-containing portion of the light chain vector to be combined with the V_H-containing portion of the heavy chain vector into a single linear vector for the coexpression of both chains. In addition to the asymmetric restriction sites, each vector includes a leader sequence for the bacterial *pel* B gene (Better et al 1988); a ribosome-binding site at the optimal distance for expression of cloned sequences; and cloning sites for either the V_L or V_H PCR products. The heavy chain vector contains a decapeptide tag at the C-terminus of the expressed V_H fragment for immunoaffinity purification (Field et al 1988).

For the synthesis of V_H and V_L sequences, polyA+ RNA is prepared from the spleen of a single immunized mouse and used in first-strand cDNA synthesis (Aviv & Leder 1972). Resultant DNA–RNA heteroduplexes are used as templates for subsequent amplification by PCR. Primers used for amplification of V_H and V_L sequences are as previously described (Huse et al 1989). V_H amplification is performed in eight separate reactions (Saiki et al 1988) with each reaction containing one of eight 5′ primers and a common 3′ primer. The 5′ primers incorporate an *Xho*I site in the PCR products and the 3′ primer incorporates a *Spe*I restriction site. These sites are used for cloning the amplified products into the heavy chain vector in a predetermined reading frame for expression.

An analogous set of PCR primers is used for the amplification and cloning of mouse κ V_L sequences. These primers incorporate *Sac*I and *Xba*I restriction sites into the PCR products for orientational cloning in the correct reading frame. PCR is performed in independent reactions using five separate sets of primers to ensure unbiased amplification of mRNA sequences. Each reaction contains one of the five 5′ primers and a common 3′ primer. PCR products are pooled and cloned into their respective vectors for the construction of separate V_H and V_L libraries.

The heavy chain library was created from mRNA isolated from the spleen of a 129 G_{IX^+} mouse previously immunized with a *p*-nitrophenyl phosphonamidate transition state antigen (NPN) coupled to keyhole limpet haemocyanin. This primary library contained 1.3×10^6 plaque-forming units (pfu) and at least 80% of the clones express the Fd fragments when assayed by

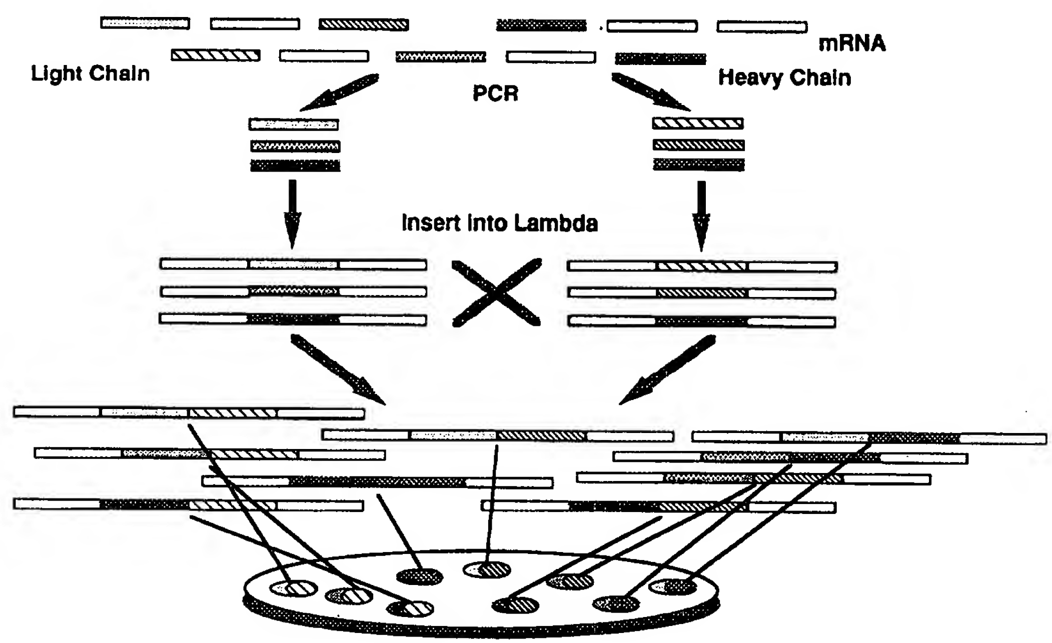


FIG. 1. Scheme for cloning V_H and V_L sequences into λ vectors then crossing the vectors to give coexpression of both chains in a single linear vector.

immunodection of the decapeptide tag. The light chain library was constructed in an identical fashion and shown to contain 2.5×10^6 members. Screening with an antibody to κ chain indicated that 60% of the library expressed light chain inserts.

A single Fab expression library was constructed by ligating the left λ arm containing V_H sequences to the right λ arm containing V_L sequences from each library. To create the library where each vector coexpresses a single heavy and a single light chain-encoding sequence, we performed step-wise restriction of the separate library DNAs to eliminate the λ arms not carrying either encoding sequence. Therefore, the only products which can join together to produce viable phage are the arms containing the heavy and light chain sequences. Light chain library DNA is first digested with *Mlu*I. The ends are dephosphorylated and then digested with *Eco*RI. Preparation of heavy chain library DNA is performed analogously, however the first digestion is with *Hind*III. Products are ligated at their *Eco*RI sites to create a coexpression library.

Reverse immunoscreening of one million phage plaques with labelled NPN coupled to bovine serum albumin (BSA) identified approximately 100 clones which bound to antigen. Antigen–antibody specificity was determined for five of the clones by competition with free unlabelled antigen. The results demonstrated that individual clones could be distinguished on the basis of antigen-binding affinity; the concentration of free antigen for complete inhibition ranged from 10 to 100×10^{-9} M. They also show the production of a recombinant antibody library which compares favourably with the *in vivo* repertoire in terms of size, diversity and antigen-binding affinities.

The mammalian repertoire is typically estimated to contain 10^6 to 10^8 different antigen specificities. Antibody libraries of this size can be obtained using standard recombinant methods and screening techniques to access this number of different molecules in a relatively short time. If more diversity is needed, heavy and light chains within the initial coexpression library or from the original single chain libraries can be systematically shuffled to give larger libraries. Reshuffling of heavy and light chains allows the generation of virtually all possible combinations of V_H and V_L pairs, since the number of individual chains within the library is smaller than the number of possible pairs. V_H and V_L chains can be represented as components of a grid (Fig. 2), with V_H chains along the top row and the V_L chains down the side column. Pairing each chain in a row with each in a column produces a matrix containing all possible combinations (Fig. 2, top). This matrix can be viewed as the total immunological repertoire within an organism. If the initial library does not contain all possible combinations but has each heavy and light chain represented in the population (Fig. 2, middle), then the entire matrix can be generated by reshuffling the chains. The three matrices in Fig. 2 (middle row) represent recombinant antibody populations which might be obtained after the initial construction of the library.

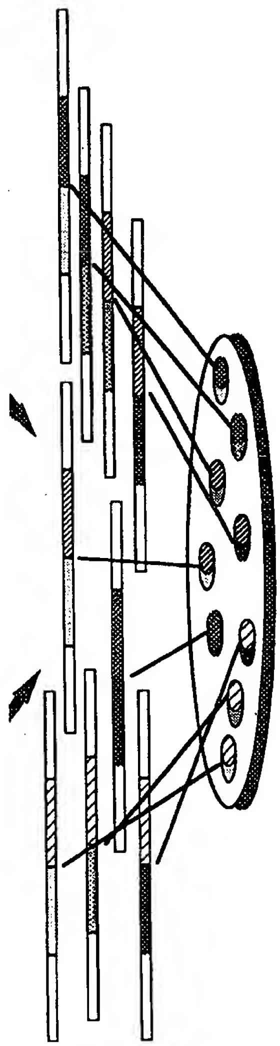


FIG. 1. Scheme for cloning V_H and V_L sequences into λ vectors then crossing the vectors to give coexpression of both chains in a single linear vector.

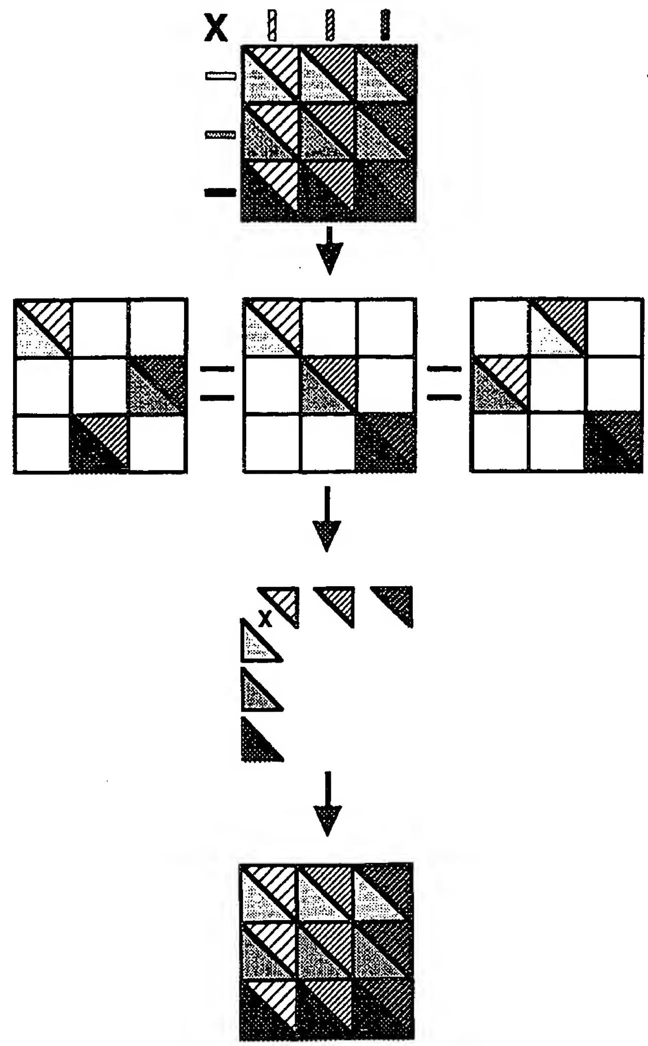
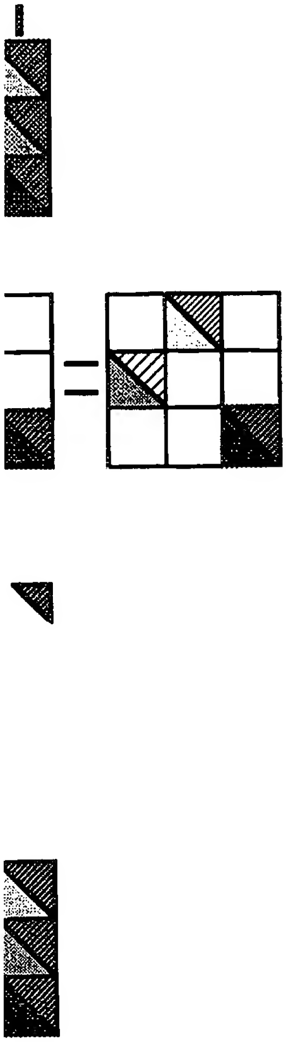


FIG. 2. Schematic representation of the way in which the complete immunological repertoire of an organism can be obtained from individual libraries that contain different subsets of heavy and light chain sequences.

Although they contain different species, the three matrices are equivalent in that each one can be generated from the other by unlinking heavy and light chain pairs and reshuffling. Reshuffling will also generate the complete repertoire of possible species (Fig. 2, bottom). Thus, recombinant libraries can be constructed which faithfully mimic the diversity characteristics of the natural immunological system.



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Recombinant antibody libraries also create a relatively unbiased distribution of possible species within the population. Inherent within the immunological repertoire will be prevalence of certain species because of factors such as favoured heavy and light chain re-arrangements and selection of particular heavy and light chain combinations by immunization of the animal. The *in vivo* repertoire has been modelled to account for these factors. Shuffling of the predominant heavy and light chains with the less prevalent chains produces a new population with different characteristics. Diversity within the population does not change, but the frequency of individual species is more equally represented. Unbiased representation of all possible species allows easy access to many more rare antibody species than could previously be obtained.

These results demonstrate that it is now possible to construct and screen several orders of magnitude more clones than using standard immunological techniques. Given the characteristics of recombinant libraries, it may now be possible to isolate antibodies to any desired antigen without immunization of live animals.

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DISCUSSION

Schultz: The primers you used have 80% homology with framework 2 sequences from the Kabat sequence collection. When we use those primers we get mis-priming in framework 2.

Huse: Is the homology with framework 2 of the heavy chain or the light chain?

Schultz: Both. In many of our PCR reactions we see two bands on the gel and one must be careful to choose the right band.

Kang: Dennis Burton and I have sequenced a group of mouse and human immunoglobulin variable regions generated by PCR using primers designed to amplify sequences from framework 1. In the case of mouse Fabs that bind NPN-hapten, we have sequenced V_H and V_L for 20 individual clones and have sequence for framework 1 of the heavy and light chains, respectively, for each one. Dennis Burton has observed the same for human V_H and V_L regions.

Huse: We have sequenced 25 randomly chosen clones. All those clones contained framework 1 sequences.

Burton: The upper bands are much higher on the gel. I am surprised if that's true in the sense of putting the decapeptide in frame.

Huse: From the homology of the amino acid sequences, you would expect the decapeptide to be in frame.

Schultz: We also get the decapeptide in frame. I have a compilation of the primers and the matches. In every case there is only a 2 bp mismatch. There is also a third reading frame containing a *lacZα* insert. Would that contribute to the translational inefficiency?

Huse: I wouldn't doubt it. It is difficult to get rid of that site in λ phage. It is very cumbersome to construct anything in λ phage. We are now making some new vectors that will not have that *lacZ* insert.

Shokat: This library is from a mouse immunized with a keyhole limpet haemocyanin (KLH) conjugate. Have you tried screening the light chain library and the heavy chain library separately against a KLH plate?

Huse: We did not test these specific libraries with KLH, but we did test some earlier ones. The problem is that KLH is sticky and when you get spots they don't replicate very well.

Shokat: Could you get heavy chain binding in the absence of light chains, or vice versa?

Kang: We screened the combinatorial library generated from mice immunized with NPN–KLH and found that the KLH sticks to everything. We have no evidence that heavy or light chains alone bind to NPN–bovine serum albumin.

Lerner: Caton & Koprowski (1990) have made a library to influenza virus haemagglutinin using combinatorial libraries. They raised antibodies to the same antigen by hybridoma technology and basically got the same antibodies. They then screened the heavy and light chains individually and did not get any binding.

Paul: That would be a function of binding affinity.

Huse: Binding below a certain affinity (I am not sure what that affinity is) would not be seen using this assay.

Paul: If the assay could detect interactions with weaker affinities, presumably you could pick up binding by single chains.

Huse: The question is, when you do find something that sticks to the heavy chain alone, is that binding specific? If it is not specific, is it predictive of a heavy chain that in combination with a particular light chain will confer specificity? I do not believe the heavy chains that bind non-specifically alone will, in combination with any light chain, necessarily become specific for an antigen.

Mountain: Can you manipulate the stringency of the probing to select for high affinity antibodies?

Huse: I would imagine so, but I don't know. The assay is probably not that sensitive. The concentration of the antibody is not well controlled in those λ phage plaques; different plaques may have very different levels of antibody expression, which will make it hard to separate differences in expression levels from differences in affinity.

Mountain: What's the evidence that you need a bicistronic arrangement of the heavy and light chain gene sequences?

Plückthun: We have used the bicistronic construct, but have also used two different plasmids: the bicistronic construct is the most efficiently repressed. This is important as the induced cells start to lyse. I don't think there is an intrinsic physical reason why the information for both protein chains would have to be on one mRNA molecule.

Mountain: It is not to do with heavy and light chains needing to be secreted in close proximity?

Plückthun: I don't think so. Secretion and folding in each other's presence are what is required, but I don't think that the proteins know whether they were coded on one or two mRNA molecules.

Paul: Dr Huse, the primers you used for amplification by PCR are derived from the amino acid sequences of a limited number of antibodies. Will these primers lead to amplification of every antibody cDNA or nearly every one?

Huse: This method will lead to isolation of the heavy chains that are normally present in the response of a mouse. Dennis Burton and Andreas Plückthun can say more about the diversity of the sequences that are isolated in terms of antibodies to a particular antigen. If we are generating a very diverse set of antibodies to a particular antigen, that would suggest that PCR priming occurs fairly universally on antibody sequences.

Burton: The impression is that you are getting an extremely large, diverse library. That could be true for non-immunized animals, but in an immunized animal, presumably the levels of mRNA from the immunized B cells are much greater, so the repertoire of antibodies generated is limited. Caton & Koprowski (1990) found that one in 200 heavy chains were identical. In the mouse the number of binding sequences is limited: in humans it is greater but still limited. As Richard Lerner has said, the hybridoma technology gives a limited number of sequences.

Plückthun: How do you check the diversity of your plaques?

Huse: From the initial library made with these PCR primers we sequenced 25 randomly chosen clones and they all had different sequences. 20–25% had only a few base pairs different; others had very unrelated sequences.

Hilvert: Gene recombination events are likely to be independent of protein structure, but there might be a structural bias against certain combinations of different heavy chains with different light chains. Is that ever seen in structures of antibodies? Are there certain classes of combinations?

Plückthun: This has been argued for a long time, but there are only a few well designed experiments that address this question. For the different types of phosphorylcholine-binding antibodies, you can obtain cross-association, but you get no antigen binding by any of the cross-associated molecules, only by the original ones. Only in some cases can we understand structurally why the antigen is not bound.

Hilvert: But do you get stable heavy and light chain dimers in the case of the non-binders?

Plückthun: That was what was reported by Hamel et al (1986).

Burton: We have seen the same heavy chain pair with different light chains and still give binding.

Huse: But a heavy chain that binds with more than one light chain still does not bind antigen when combined with most available light chains.

Lerner: If you mutate the framework regions of the antibodies, you get individual specificities. People would argue that in the very high affinity antibodies, not only have you mutated the loops, you have also mutated the dimer interface. Those structures that don't fit any longer drop out. The people who study this effect would argue that private associations occur in less than 5–10% of the very high affinity antibodies.

Hansen: Are any of the antibodies that you raised against the transition state analogue catalytic?

Janda: The problem is that not much protein is produced. Although several different reactions have been catalysed by antibodies, most of the reactions require large amounts of antibody (e.g. 5–20 μM). We have begun to screen some of the antibodies from the library to the nitroanilide phosphonamidate. We began with 20 and have identified one tentatively that cleaves the ester but not the anilide. It must be different from antibody 43C9 because the latter cleaves

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both the anilide and the ester. We have the DNA sequence of each antibody, so we can see the differences between them.

Hansen: Have you made a library against a transition state analogue that gave a much higher hit rate in the traditional immunization procedure? By traditional immunization, this analogue yielded one catalytic antibody out of 50 you studied; if you are seeing zero out of 20 that could be consistent with the numbers you had before.

Janda: The idea was that by using the library we could find a much greater number of hits.

Schultz: When you screen against that particular hapten for catalysis, won't you run into problems with bacterial enzymes?

Lerner: You can't screen plates for ester and amide hydrolysis. We've tried periodically to screen for substrates in the agar but the bacterial lawn alone often causes the plate to change colour.

Schultz: We're looking at using D esters or amides to do these screens.

Huse: The underlying question is the desirability of doing the assay for catalysis directly without screening for binding initially.

Janda: You would have to have an antibody with a huge turnover number.

Schultz: Or an extremely sensitive assay. We have built into our hapten a fluorescence energy transfer assay which is extremely sensitive.

Lerner: Phage plaques are often screened by enzymic assay, for example the release of halogenated indoles, but β-galactosidase is a very efficient enzyme.

Jencks: Do you have a rough estimate of the affinities of the heavy and light chains compared to that of the intact molecule?

Huse: We don't see anything with the heavy and light chains separately.

Lerner: The problem with heavy chains is they like to stick to things, including light chains and plastic. It is very difficult to study heavy chains alone.

Plückthun: We find exactly the same thing, both the V_H domain alone and the whole heavy chain of the Fab fragment have real problems with solubility. Therefore I am sceptical at least about the generality of using these as antibody substitutes. I don't want to deny that it may work in some cases, but if it's not general, it may not be so useful.

Lerner: The only formal experiment that has been done is that of Andrew Caton. He made a library to a protein molecule, not a small hapten. He divided the library in half and did not see any binding. He could have had, according to the DNA sequences, one in 200 of the heavy chains as proper binders but looking at a million he didn't see any.

Huse: One reason for looking at heavy chains alone was that it was not possible to look at the heavy and light chains together. Hopefully, that is not going to be an issue in the future.

Paul: I am having difficulty relating this discussion to work done in the 1960s and early 1970s. The antibody paratope is a complex of V_H and V_L. Dissociated antibody chains could possess either reduced or no antigen binding

activity. It was shown by immunochemical methods that single chains can bind antigen: heavy chains were found to bind better than light chains (Franek & Nezlin 1963, Porter & Weir 1966, Utsumi & Karush 1964). More recently, Greg Winter and co-workers showed that recombinant V_H binds lysozyme (Ward et al 1989). The single chains have reduced binding affinity, but there is little doubt that it is true binding rather than non-specific 'stickiness'.

Huse: The two cases are different. In the first, you take antibodies that bind antigen and ask if their isolated heavy chains have any residual affinity. In the second, you take isolated recombinant heavy chains that stick to an antigen. One would like to know if these are the same population as in the first case. I believe the isolated heavy chains in the second case are probably ones that had residual affinity in the first case plus a bunch of others that are just plain 'sticky' and have nothing to do with specific antibodies. This 'stickiness' could give a background signal that overwhelms the small signal from the residual affinity of heavy chains in the first case.

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Screening combinatorial antibody libraries for catalytic acyl transfer reactions

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Abstract. A bacteriophage λ vector system for the expression of Fab fragments from the mouse antibody repertoire in *Escherichia coli* has been described. We have used this system to generate a catalytic antibody from a combinatorial antibody library. Monoclonal antibody 43C9 was raised against a transition state analogue of the hydrolysis of carboxyamide. mRNA from hybridoma cells expressing this antibody was cloned into phage λ and clones that expressed the mRNA for either the heavy or the light chain of the antibody were isolated. These individual libraries were then crossed to generate a combinatorial library in which clones coexpressed the heavy and light chains. This library was screened for antibodies/Fab fragments that bound to the original antigen with high affinity. DNA sequencing showed that these fragments were the same as those in antibody 43C9. Three different clones were found to catalyse the hydrolysis of carboxyamide. More efficient expression vectors and improved screening techniques should lead to the isolation of many more catalytic antibodies from combinatorial antibody libraries.

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Monoclonal antibodies are used extensively in various fields of biology and medicine. Some important applications include the investigation of cellular mechanisms, the isolation of interferons, cancer research, clinical diagnosis and gene product analysis. The generation of monoclonal antibodies with specific catalytic functions is an emerging technology that combines the high specificities of antibodies with chemical catalysis. A number of reactions have been successfully catalysed by monoclonal antibodies (for review see Lerner & Benkovic 1988). The production of homogeneous antibodies for catalysis is entirely dependent on the hybridoma technology; but this is an inefficient method

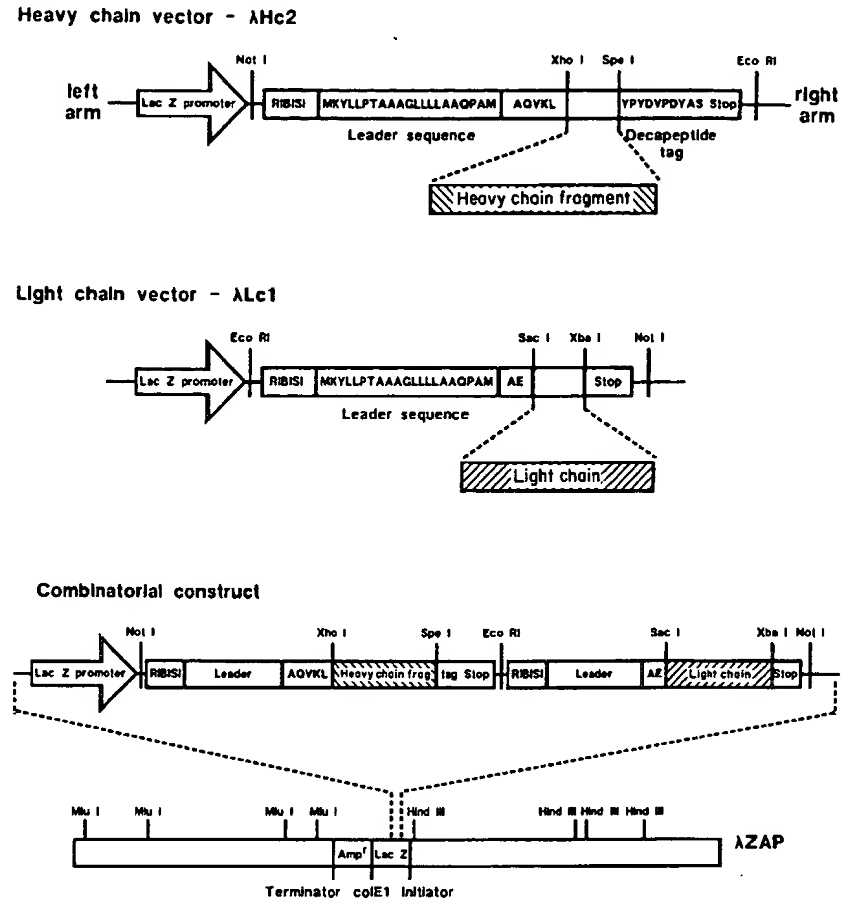


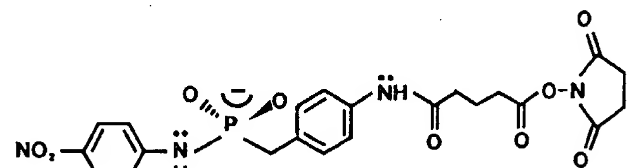
FIG. 1. Combinatorial bacteriophage λ vector system for expression of Fab antibody fragments. The LC1 vector is for cloning PCR products of mRNAs that code for κ light chains; the HC2 vector is for cloning PCR products of mRNAs coding for heavy chain Fd sequences. The combinatorial constructs that can express Fab fragments are generated by cutting light and heavy chain DNA at the antisymmetric *Eco*R1 site of each vector, followed by religation of the resulting arms.

for surveying the immunological repertoire and limits the number of catalysts that can be obtained. We have developed a system using bacteriophage λ to clone and express a combinatorial library of Fab fragments of the mouse antibody repertoire in *Escherichia coli* (Fig. 1) (Sastry et al 1989, Huse et al 1989). The system allows rapid and easy identification of monoclonal Fab fragments in a form suitable for genetic manipulation. However, it remains to be shown that such combinatorial libraries can be used to produce catalytic Fab

fragments. In this paper we demonstrate the generation of a catalytic antibody from a combinatorial antibody library.

Using the λ phage system we generated an Fab combinatorial library from the spleen of a mouse immunized with phosphonamidate **1** (NPN), a transition state analogue for the hydrolysis of carboxyamide substrate **2** (Fig. 2). Screening the library with the antigen, NPN, linked to bovine serum albumin (NPN-BSA) resulted in the identification of a number of Fab fragments that bound to the antigen in a competitive manner. To find efficient catalysts for the hydrolysis of the nitroanilide **2**, we screened the Fab combinatorial library directly for catalysis. The induced phage libraries were incubated with nitrocellulose filters saturated with the substrate, or the substrate was added directly to agar containing cells infected with the phage before they were poured onto a plate. Unfortunately, these approaches were unsuccessful because of the chemical nature of the reaction as well as the limited amount of Fab that is secreted by the phage molecules. It has previously been observed that catalysis of hydrolysis of the amide **2** occurs at 37 °C with high concentrations of an antibody (Janda et al 1988).

The high concentrations of antibody required for catalysis are difficult to achieve directly on the phage surface. Also, the product of the hydrolysis, *p*-nitroaniline, is diffusible and is hard to observe either directly on phage



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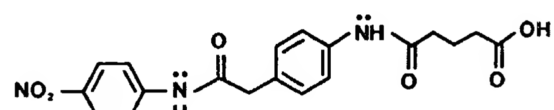

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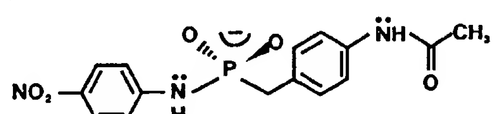

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FIG. 2. The transition state analogue phosphonamidate **1** (NPN) which was used to induce antibodies that hydrolyse the carboxyamide substrate **2**. The phosphonamidate functionality mimics the stereoelectronic features of the transition state for hydrolysis of the amide bond. The transition state analogue **3** is an inhibitor of the reaction.

plaques or on nitrocellulose filters. Because of these practical limitations, we decided to screen initially for Fab fragments that bound to NPN and then for those that showed catalytic activity. As an essential first step, we cloned and expressed a monoclonal antibody (43C9) that catalyses the amide hydrolysis in the phage system (Janda et al 1988). Besides being an internal control, the expression of the monoclonal antibody in phage also allows the study of its structure and mechanism of catalysis. Mutagenesis and chain-exchange experiments can be easily performed on the cloned antibody to improve its catalytic activity.

Methods

Total RNA from 10^7 43C9 hybridoma cells was isolated as described (Chomczynski & Sacchi 1987). The mRNAs were purified on an oligo dT column, then amplified using the polymerase chain reaction to obtain separate pools of heavy and light chain DNA (Sastry et al 1989, Huse et al 1989). Amplification of heavy chain DNA was performed with eight different 5′ primers and a 3′ primer specific for the IgG2b isotype. Light chain DNA was similarly amplified with five 5′ primers and a κ chain-specific 3′ primer. Heavy and light chain libraries were generated in phage λ and crossed to obtain an Fab combinatorial library (Huse et al 1989). This library was then screened with NPN-BSA labelled with ^{125}I and Fab fragments that bound the antigen were identified (Huse et al 1989). These Fab fragments were excised using helper phage (M12 mp8) and McBlue cells and plated on LB/ampicillin plates (Short et al 1988). Colonies on the plates represented the excised plasmid carrying the cloned heavy and light chain pieces.

Individual clones were grown up and their protein products isolated using an affinity column made from anti-$(Fab')_2$ coupled to Sepharose beads. Purified Fab was dialysed for 4–6 hours against ATE (Aces, Tris, ethanolamine) buffer, pH 9.0, concentrated to 1–3 μM solution, and used for catalysis. Catalysis was performed at 37 °C in ATE buffer at pH 9.0 with the 1–3 μM Fab solution and a saturating amount (1 mM) of substrate **2**. Sequencing of the positive clones was as described by Sanger et al (1977).

Results

PCR amplification of heavy and light chain DNA resulted in bands of about 700 bp as analysed by agarose gel electrophoresis. A number of different primers were used for amplification from the hybridoma cells, because these may contain other non-functional heavy or light chains and restricted amplification may result in the cloning and expression of the wrong chains. To avoid this problem, we pooled the amplified DNA from the heavy and the light chains, then cloned each pooled fraction into the expression vector. Cloning of heavy chains resulted in 2×10^6 recombinants; the light chain library contained 5×10^5 recombinants.

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Screening of the heavy chain recombinants with an antibody raised against a conserved 10 amino acid sequence in the heavy chain showed that 90% of these were expressing the decapeptide and therefore the heavy chain. Anti-κ antibody screening of the light chain library indicated that 60% of the clones were expressing κ light chains. The combinatorial library consisting of 2×10^7 recombinants was screened with the anti-decapeptide and anti-κ antibodies; 65% of the clones coexpressed heavy and light chains.

The Fab library (3000 plaques/plate) was then screened with iodinated NPN-BSA and positive clones were identified after a three-day exposure. Fragments that bound the antigen (binders) were identified at a frequency of 1/200; this relatively low frequency may be due to the presence of non-functional heavy and light chains in the Fab library. Ideally, amplification of the hybridoma RNA with specific 5′ heavy and light chains should generate Fab fragments that bind at a much higher frequency.

The DNA sequences of the binders were obtained to identify the clone that exactly represents the monoclonal catalytic antibody 43C9. Comparison of the light chain deduced N-terminal amino acid sequence of antibody 43C9 and the deduced amino acid sequences of ten of the binders indicated that five of the clones (8a11, 8a12, 8a1, 7a2, 7a4) had the correct light chain. Three of these clones (8a1, 8a11, 8a12) were identical and differed from each of the other two (7a2, 7a4) by a single amino acid in the framework region. All the clones had the same heavy chain sequence; comparison with the N-terminal sequence of the authentic antibody was not possible because its N-terminus is blocked.

Purified Fab from each of the ten clones described above was assayed for catalytic activity; 8a11, 7a2 and 7a1 hydrolysed amide **2** at a rate clearly above the background rate (Fig. 3). The reaction was inhibited completely by the addition of transition state analogue **3**, 20 μM. This indicated that the observed catalysis was exclusively due to the Fab. SDS-PAGE of the catalytic recombinant Fabs showed a single species at 50 kDa. Reducing conditions gave a doublet at 25 kDa, indicative of a single pure Fab fragment. Because of the limited amount of Fab produced in our system, detailed kinetic analysis has not been possible. Overexpression of the catalytic Fab is currently being sought, to facilitate the kinetic studies.

Discussion

The bacteriophage λ vector system developed for the expression of Fab fragments is ideally suited for studying the structure and mechanism of any desired monoclonal antibody. We have successfully expressed a monoclonal catalytic Fab in this system and have shown that it retains the ability to catalyse a specific amide hydrolytic reaction.

Future studies will be aimed at identifying more binders from the library which also display catalytic activity. The success of these will hinge upon our ability

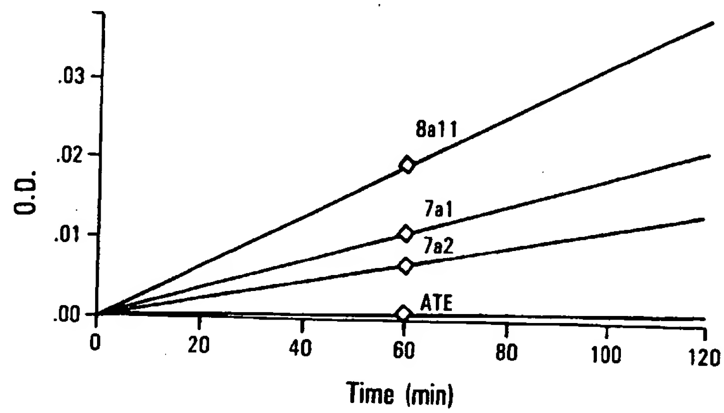

FIG. 3. Hydrolysis of carboxyamide 2 by Fab clones 8a11, 7a2 and 7a1. Hydrolysis was carried out at 37 °C with 2 μM antibody, 1 mM substrate in ATE buffer, pH 9.0. The differences in the observed rates seen for each clone probably reflect inaccuracies in protein concentration determination rather than clone differences. The background hydrolysis was measured with the substrate alone; in all cases the reaction was monitored at 405 nm.

to obtain a better system for expressing the protein, possibly utilizing Summer's baculovirus system (Smith et al 1983). More efficient screening for catalytic antibodies might be achieved via a genetic selection process.

Finally, a general solution to the antibody catalysis of a peptide bond may be obtained using the phage technology presented. Recently, we have constructed a single chain antibody with a coordination site for metals (Iverson et al 1990). When this site is incorporated into the light chain of an Fab fragment, a bound metal ion could act as a hydrolytic cofactor when properly aligned with a heavy chain which binds a small peptide sequence. The possibility of such a reaction appears remote; however, by taking advantage of the large numbers and combinations available through the combinatorial library, opportunities for success are within reach.

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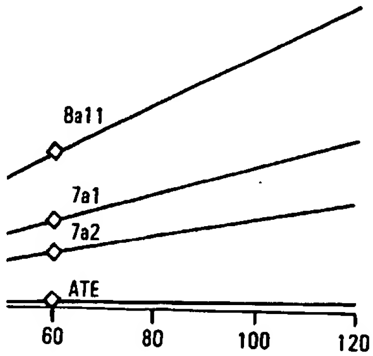

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DISCUSSION

Hansen: The exact placing of an amino acid is critical for enzyme catalysis. Do you have a sense, perhaps from Sargeson's work (Buckingham et al 1970), of how precise one has to be in orienting a carbonyl group near the metal ion to see catalysis?

Lerner: I don't know. They were basically looking at an intramolecular situation, because the substrate was directly bound to an open site on the coordination complex.

Martin: Another structural detail to consider is the geometry of the antibody's metal-binding ligands. A slight difference in the relative positions of metal-binding amino acid side chains could have a dramatic effect on the catalytic efficiency of the antibody. The coordination geometry of metals in natural enzymes is often distorted: for example, the tetrahedral geometry of cobalt-substituted carboxypeptidase A is markedly irregular compared to simple tetrahedral complexes of cobalt such as cobalt tetrachloride. In their entatic state hypothesis, Vallee & Williams (1968) proposed that the distorted coordination geometry is a critical feature of metalloenzymes in that it causes the metal to be unusually reactive—in their terms 'poised for catalysis'.

Lerner: Isn't that flying in the face of results from a great number of coordination complex experiments?

Jencks: Ground state strain of that kind can change the properties of the ions and the ligands and the metal, certainly; but to say that the ground state strain or distortion directly influences the transition state is wrong. It may provide a system which has a proper p*K* or oxidation potential or whatever, that will lead to a transition state more readily, and this might be done better with another metal that has a different size and a different potential, but it doesn't relate directly to the stability of the transition state.

Martin: If the enzyme or antibody binds a metal with tetrahedral geometry, say by three amino acid side chains and a reactive water molecule, the effect of the distorted coordination geometry might be to fine tune the p*K* of the metal-bound water molecule, thereby making it more reactive.

Hansen: In the crystal structure of the metalloantibody (Iverson et al 1990), are there any peptide bonds of the antibody itself near the metal ion which might cause autodecomposition?

Lerner: We tried to do that experiment with copper(II). We think we have seen rather restricted proteolysis, but that uses other copper coordination sites outside the binding pocket of the antibody.

Plückthun: Have you looked at the effect of the presence of the metal ion on the folding of the protein?

Lerner: Yes. The protein can re-fold with and without the metal.

Plückthun: Are you surprised that the metal gets in and out so easily?

Lerner: No; it does so in enzymes. We were careful to do the whole experiment in metal-free water, because we didn't want any extraneous metals to get into the site.

Schultz: There is a phenolic oxygen fairly close to the metal ion in the antibody combining site. Have you looked at hydrolysis of fluorescein esters?

Lerner: No.

Iverson: We tried fluorescein diacetate and obtained no rate enhancement for the hydrolysis of this compound by the antibody in the presence or absence of the metal.

Lerner: But in terms of other partners for coordination, which Peter Schultz is asking about, there is another possibility, namely an aspartate that could be a coordination partner.

Suckling: Have you looked for electron transfer reactions in any metalloantibodies?

Lerner: Not yet, but we hope to.

Wilson: Have you tried a general screen with peptides to see whether any other antigens bind, as Scott & Smith (1990) did?

Lerner: No; it would be very interesting to do. Raymond Dwek's lab found a metal-binding site in a known antibody. If one is interested in accidents, one ought to screen catalytic antibodies, plus and minus metal. But metals can also make enzymes function considerably worse!

Jencks: I suspect you have thought of a good many things that metals will do, when they are attached to antibodies. Would you say any more on what you think about doing in the future?

Lerner: We plan to try to solve the so-called 'pre-monensin syndrome', which means how many chemist man hours are required to make monensin from pre-monensin, the problem being that there are so many chemically identical alkenes. We want to selectively epoxidize those molecules to do stereochemistry. We also, like Peter Schultz, want to try oxygen transfer reactions, particularly hydroxylation of steroids.

There are two important things to be done. One is to use these metalloantibodies for asymmetric inductions, where one would not have to use chiral auxiliaries because the antibody would give the system its asymmetry.

The success of that approach depends on (1) the binding specificity, and (2) how much trouble we shall have when we use relatively strong reagents like peracids.

Secondly, the single most important experiment one could do, thinking of the medical applications, is the selective cleavage of peptide bonds, using a recognition unit of seven amino acids rather than one or two. Proteases are relatively promiscuous enzymes and depend in part on the site environment rather than on the sequence of amino acids. One could not inject trypsin, for instance, into a person because it's too promiscuous. The ability to position ZnOH selectively in relation to seven amino acids would be tantamount to developing a restriction enzyme for protein molecules.

Benkovic: We also provide spectroscopists with a chance to investigate copper environments. There is a scarcity of models for copper(I) and copper(II) in various binding sites: by having a system that we shall be able to characterize by X-ray crystallographic analysis and manipulate at will, we should obtain interesting spin echo and electron paramagnetic resonance spectra for copper in these kinds of sites.

Lerner: If one is also interested in the flight of the electron in the protein cavity, there is no reason why one couldn't put two metals in there at defined distances and measure the rates of electron transfer.

Schultz: Could one use metal ion detoxification (such as HgII resistance) as the selection pressure to induce antibodies that have a metal-binding site?

Lerner: I think so. People have similar concepts to what you are talking about for immunization with alkylating agents: what if you were to immunize with a compound containing an open coordination site, such as HgII?

Hansen: The prospect of peptidases with more restricted recognition sites is very exciting. On a specific point, where is the metal ion in relation to the seven amino acid binding cleft that you mentioned?

Lerner: I don't think one can generalize about this. Because Ian Wilson is our neighbour, we have looked very closely at what we could do to cut a peptide in complexes whose structure he has solved. I don't believe a metal site would be close enough to any of the peptides that he has in his X-ray crystal structures to deliver the hydroxyl group effectively.

Hansen: The reverse question is whether the metal site would block peptide binding.

Lerner: If you look at the site in a 'cut-away' view, and if you assume that the peptide goes into it like a straight molecule, which it probably does not, it would not be easy to approximate a scissile bond, let's say next to a ZnOH. So you might wish to go further up the site. An antibody molecule often has a groove that could accommodate a peptide. I can imagine that the peptide will lie in that groove and approximate a scissile amide to the zinc ion. However, it remains to be shown that the present construction is good for peptide bond cleavage.

Hansen: Is the binding constant such that the metalloantibody holds together at zero metal concentration?

Lerner: The formation constant for CuII is micromolar. The constant for zinc is unknown.

Hansen: What about using a metalloantibody *in vivo*, therapeutically?

Lerner: At the moment one would have to pre-load. If the disease you want to cure is critical, you could infuse both the antibody and the zinc into the patient to increase the *in vivo* concentration of zinc. You could not do this with copper or other more toxic metals.

We hope soon to finish the coordination chemistry of the L1-L3 site, where we have tried thiols and carboxylates. I would be pleased to get a coordination constant of 10^8–10^9 there. There are many permutations of those three side chains that one needs to look at.

Harris: Many proteins have calcium associated with them. Have you thought about trying to introduce calcium-binding sites into antibodies?

Lerner: Steve Benkovic pointed out to me that when a protein binds carbohydrates it tends to use calcium. It's very difficult to make an antibody with a good binding constant for carbohydrate. Elvin Kabat said that he had never seen one better than millimolar. So to build an antibody that binds a carbohydrate, one might do as you suggest.

Harris: Calcium binding occurs via aspartate residues: where would be the best site for those to be placed?

Lerner: We are making 3-Asp and 3-Glu sites to see how those work.

Paul: You mentioned that R. Dwek's group had a monoclonal antibody with a metal-binding site, is it known where the metal is bound?

Janda: R. Dwek and co-workers found that the MOPC315 antibody bound lanthanides (Dower et al 1978). The antibody was pretty well characterized by Steve Dower (1978). He found that two carboxylates bound a lanthanide in addition to binding a *p*-nitrophenyl phosphate as a reporter molecule.

Burton: I wonder if you should make so much of this; lanthanides bind to a number of sites on antibodies, including one on Fc.

Lerner: It is not going to be difficult to build good coordination sites. What is going to be hard is approximating the metal to the substrate.

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Recombinant Polyclonal Antibody Libraries

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Abstract: We describe a technology for generating recombinant polyclonal antibody libraries (PCALs) that enables the creation and perpetuation of standardized mixtures of polyclonal whole antibodies specific for a multiantigen (or polyantigen). Therefore, this technology combines the advantages of targeting multiple antigenic determinants -- high avidity, low likelihood of antigen 'escape variants', and efficient mediation of effector functions, with the advantages of using monoclonal antibodies -- unlimited supply of standardized reagents and the availability of the genetic material for desired manipulations. The technology for generating recombinant polyclonal antibody libraries begins with the creation of phage display Fab (antibody) libraries. This is followed by selection of sublibraries with desired antigen specificities, and mass transfer of the variable region gene pairs of the selected sublibraries to a mammalian expression vector for generation of libraries of polyclonal whole antibodies. We review here our experiments for selection of phage display antibody libraries against microbes and tumor cells, as well as the recent literature on the selection of phage display antibody libraries to multiantigen targets.

INTRODUCTION

The antibody response of vertebrates to most antigens is polyclonal and targets multiple epitopes on the antigen surface [1,2]. This characteristic has co-evolved with the effector mechanisms mediated by the Fc regions of antibodies -- such as complement binding with production of C3b, opsonization/phagocytosis, and antibody-dependent cellular cytotoxicity (ADCC) -- that serve to eliminate the antigen [1-4]. Thus, triggering of effector functions requires a high density of antibodies on the antigen surface for sufficient cross-linking of Fc receptors on effector cells and for efficient C1q binding [5-7]. When the immunogen is a living cell, such as a microbe or a tumor cell, the polyclonality of the antibody response helps guard against the development of cell 'escape variants' that are no longer recognized by the antibodies. This is because the chance that a given cell will simultaneously lose all the target epitopes is (in most cases) essentially zero.

Passive immunotherapy with serum-derived polyclonal antibodies has been used for many years. The use of polyclonal human immunoglobulin (human gamma globulin) -- for the treatment of patients with agammaglobulinemia, immunocompromised patients, and patients with severe microbial infections -- is generally effective and shows no adverse reactions [8-13]. Treatment of mice with serum-derived murine polyclonal antibodies has been shown to prevent development of a murine tumor [14]. Furthermore, occasional successful treatment of human malignancies, such as melanoma and renal cell carcinoma, with polyclonal antibodies derived from animals or from humans has been reported [15,16].

Despite their efficacy in many applications, the use of conventional polyclonal antibodies is limited by: short supply of serum antibody from immunized animals or from humans; inability to modify the antibodies because the genes are not available; and, in cases where a human cell population (malignant or normal) is targeted, the likely loss of the vast majority of the antibody population if negative selection were performed to eliminate major cross-reactivities with other tissues or cell populations. This is because many cell surface antigens are expressed on many different cell types.

Unlike polyclonal antibodies, monoclonal antibodies provide an unlimited supply of standardized reagents [17-19], and their heavy (H) and light (L) chain genes can be readily cloned and manipulated. However, monoclonal antibodies target single epitopes. Therefore, they are much less efficient at activating effector mechanisms than

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polyclonal antibodies (hence the need for toxic tags in therapeutic applications [20-23]. Furthermore, the likelihood of cell 'escape variants' -- that are no longer recognized by the antibody -- is much higher for monoclonal than polyclonal antibodies.

To combine the advantages of polyclonal and monoclonal antibodies, we have developed a technology for generating polyclonal antibody libraries. This technology enables the perpetuation of standardized mixtures of polyclonal antibodies specific for an antigen or a multiantigen target (a polyantigen). Hence, it combines the advantages of targeting multiple antigenic determinants (high avidity, low likelihood of antigen 'escape variants', and efficient mediation of effector functions) with the advantages of using monoclonal antibodies (unlimited supply of standardized reagents, and the availability of the genetic material for desired manipulations such as the replacement of mouse constant regions by human constant regions to generate chimeric antibodies [24,25].

The generation of polyclonal antibody libraries with desired specificities is made possible by the technology for displaying Fab antibody fragments on the surface of phage particles to generate so called "Fab phage display libraries" [26-29]. In this system the genetic material encoding Fab fragments is obtained from the B lymphocytes of immunized animals (or from humans) and cloned into a phagemid vector such that the genetic material encoding the Fab is attached to the genetic material encoding a phage coat protein. (Fab is comprised of 2 chains: the L chain and the Fd chain. The L chain contains the variable [V] and constant [C] region [VL-CL]; and the Fd chain contains the V region and the first H chain constant domain [VH-CH1].) On transformation of bacteria with these phagemid vectors (and superinfection with helper phage), phage particles that display Fab on their surface are generated because the Fab is embedded in the phage coat via the coat protein to which it is attached. Because each phage particle contains a different vector molecule for its genome, each phage particle displays a different Fab on its surface. Phage libraries larger than 10^8 different members can be generated. The libraries can be selected for binding to specific antigens (positive selection) by affinity chromatography [30-32], including panning on antigen-coated surfaces [29].

The beauty and power of the phage display system is the coupling of a selectable function (binding to an antigen) to the genetic material that encodes that function. This is because the selected phage have a replication function and therefore a few phage particles can be amplified indefinitely if they are used to infect the bacterial host. This powerful system has been used by other investigators to select and clone-out phage encoding monoclonal antibody fragments to haptens, proteins, viruses, and cancer cells [33-42] as an alternative to the hybridoma technology.

In contrast, our laboratory has adapted the Fab phage display system to generate polyclonal antibodies (PCALs, pronounced "P"-"Cals") [43-47]. Instead of isolating monoclonal Fab phage particles, the Fab phage display libraries are maintained as polyclonal mixtures and subjected to positive and negative selection; positive selection to recover those phage particles with desired antigen specificities, and negative selection to remove those phage particles with undesired specificities (for example those with certain cross-reactivities). After amplification of the selected sublibraries, the selected antibody genes are transferred, in mass, from the phage vector population to a mammalian vector that provides complete constant region genes and appropriate transcription regulatory elements for expression of whole, glycosylated IgG antibodies in mammalian cells. Thus, the library that was selected at the Fab phage display level can be expressed -- after transfection of the mammalian vector population into mammalian cells -- as a library of polyclonal whole antibodies that can mediate effector functions. Because the transfected cells are immortal, the cell population producing the IgG polyclonal library can be perpetuated indefinitely, just like hybridoma cells. Alternatively, this cell population can be recreated as desired by transfection of the mammalian vector population into mammalian cells [Fig. (**1**)].

Polyclonal antibody libraries can be manipulated to eliminate undesirable specificities and have the unique advantage (not shared by conventional polyclonal antibodies) that desired specificities can be amplified. Thus, even if 99.99% of the antibody population to cancer cells is lost by absorption with normal cells, a library of 10^8 members will be reduced to 10^4 members, which could be amplified to generate unlimited supplies of the (still large) sublibrary. By comparison, a conventional polyclonal antibody preparation will be essentially lost after absorption to remove major reactivities against normal human cells.

PCALs (obtained by mass antigen-selection and mass transfer of selected variable region gene pairs without isolating or characterizing individual library members) differ from collections of monoclonal antibodies (each of which had been selected for

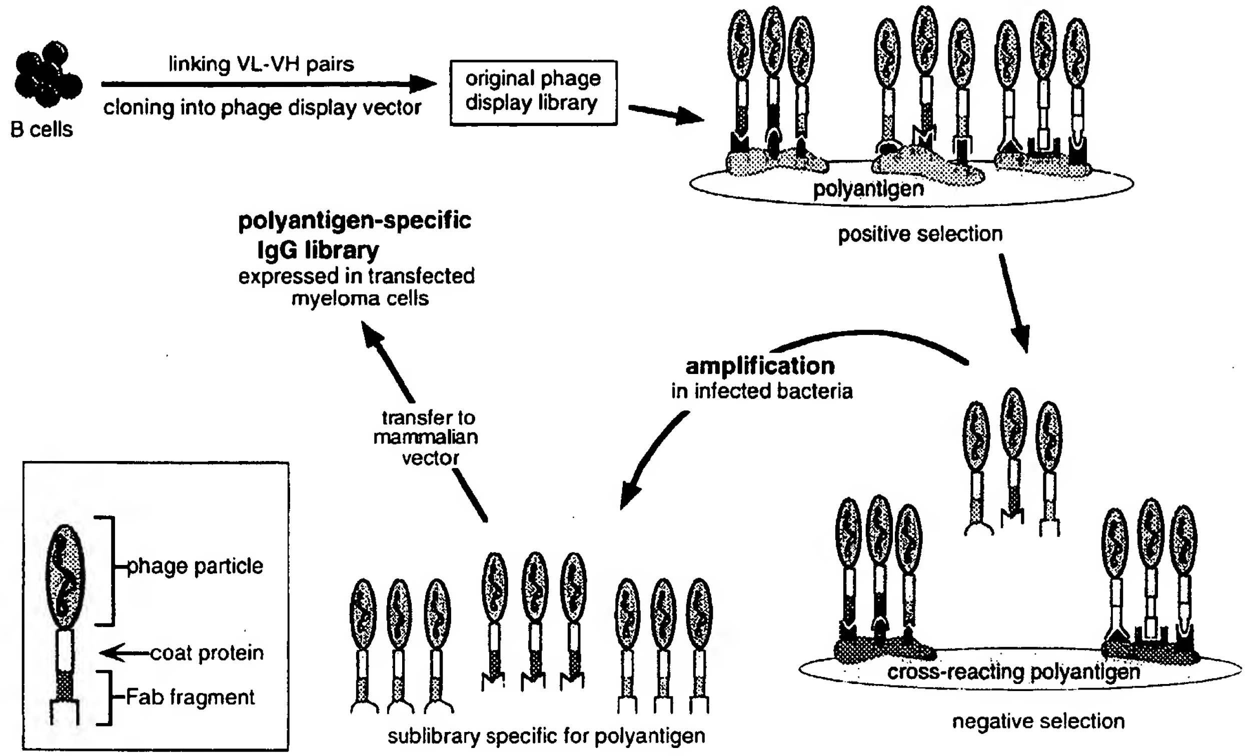

Fig. (1). Scheme for production and selection of a polyantigen-specific polyclonal antibody library.

antigen specificity). This is because PCALs contain individual antibodies which may or may not be specific for the target, but the collection of the individual antibodies recognizes the target antigen way above the background of any cross-reacting antigen, with a high signal-to-noise ratio. This concept is exemplified schematically in Fig. (2).

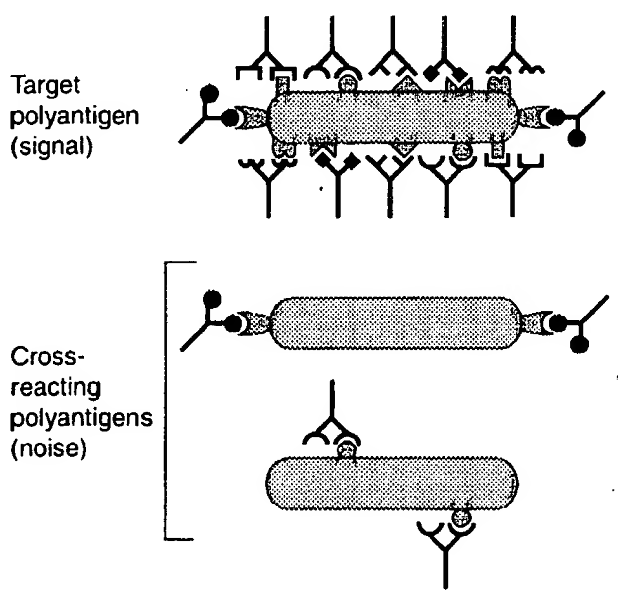

Fig. (2). Schematic representation of target recognition with high "signal-to-noise" ratio. (Although not shown, the cross-reacting polyantigens have additional antigens on their surface, that are not shared with the target polyantigen.)

THE SYSTEM FOR GENERATION OF PCALs

We have developed a system of phagemid and mammalian bidirectional vectors that facilitates the mass transfer of linked VL-VH region gene pairs [43,44], from antigen-selected sublibraries, without loss of the VL-VH combinations. The key feature of the transfer is that the VL and VH region genes are linked head-to-head (←→) in opposite transcriptional orientations. Linking of VL and VH region genes is done by reverse transcription - polymerase chain reaction (RT-PCR).

Primers, cDNA Synthesis, and VL-VH cDNA Linking

A method for cDNA synthesis and VL-VH cDNA linking was developed, and appropriate V and C region primers were designed [44,45]. In this method, RNA is obtained from B cell and plasma cell-containing tissues of immunized mice and used to prepare combinatorial libraries of VL-VH region gene pairs, linked head-to-head (←→)

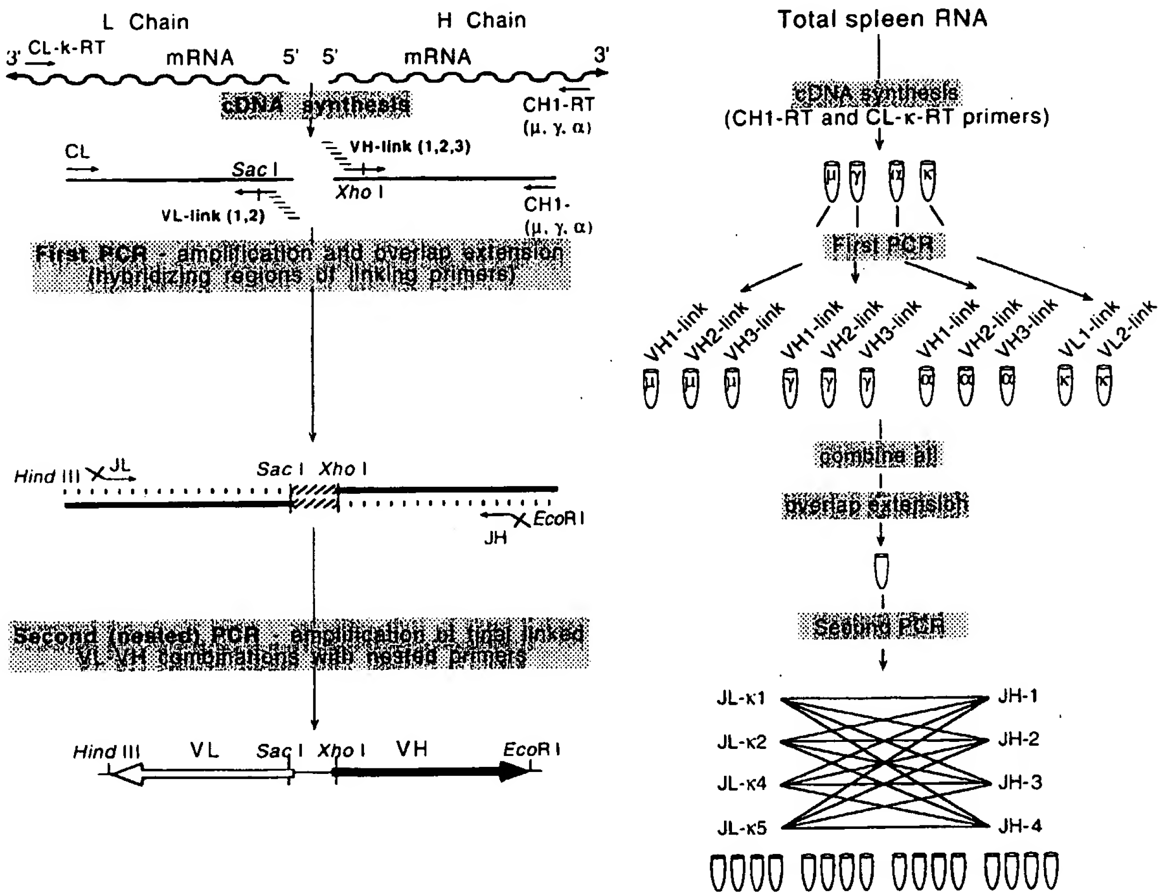

Fig. (3). General scheme for linking and amplifying VL-VH region gene pairs in opposite transcriptional orientations. VL-VH products are obtained after cDNA synthesis and consecutive PCR steps. See Fig. (4) for primer sequences.

in opposite transcriptional orientations. The general scheme for RT-PCR and linking of VL-VH region gene pairs is shown in Fig. (3). First strand cDNA synthesis of VL and VH region genes is done in 4 different tubes, each containing a different reverse primer hybridizing to μ H chains, to γ H chains (of all four mouse γ isotypes), to α H chains, or to κ L chains. The first strand cDNA library from each of the four tubes is then used in 3 (H chain) or 2 (L chain) PCRs using μ, γ, α, or κ nested reverse primers and a forward primer that hybridizes to the 5' end of VL or VH region genes. Each VH or VL primer provides a tail (link) for VL-VH linking that includes a restriction enzyme site (*Sac* I and *Xho* I for the 2 VL and 3 VH primers, respectively) necessary for subsequent insertion of promoter and leader sequences. The tail of VL primers is complementary to the tail of VH primers [see Fig. (4) for primer sequences]. Because of the relatively large number of mismatches (to prospective templates) in this minimal set of V primers, the First PCR is done under very low stringency conditions (37°C). However, subsequent steps involve PCR using nested primers at high stringency to ensure that only Ig sequences are amplified [45].

The PCR-amplified L and H chain sequences are combined into a single tube, to allow hybridization of the complementary VL and VH tails and overlap extension to generate head-to-head-linked VL-VH region gene pairs. The product of the overlap extension reaction is then used in an array of 16 separate PCRs, each amplified with a different pair of JL and JH primers that hybridize to the four Jκ and four JH mouse genes and which contain a *Hind* III or *EcoR* I site for the JL and JH primers, respectively [see Fig. (3) for scheme and Fig. (4) for primer sequences].

Generation of Fab Phage Display Libraries in a Bidirectional Phagemid Vector

A bidirectional phagemid vector was generated by modification of the unidirectional Fab phage

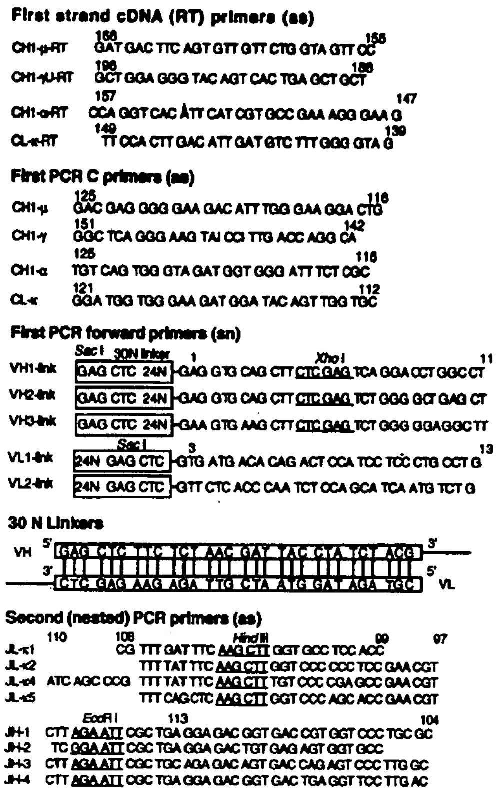

Fig. (4). Oligonucleotide primers used for library construction. The antisense and sense strands are denoted by "as" and "sn", respectively. Restriction sites are underlined. Corresponding amino acid numbers in the Kabat system [77] are shown above the sequences. Linker regions (the 30 nucleotide tails plus the first nucleotide of the VL or VH region) are indicated. N, nucleotide(s).

display vector pComb3 [29]. The bidirectional vector [48 phh3mu-γ1, Fig. (**5a**)] contains, in opposite transcriptional orientations, a moue Cκ gene and a mouse (γ1) CH1 gene segment attached to DNA encoding the carboxyl terminal end of the phage coat protein cpIII [44]. VL-VH region gene pairs linked head-to-head, in opposite transcriptional orientations, are cloned between the *Hind* III and *EcoR* I sites of the phh3mu-γ1 vector [Fig. (**5a**)] to generate a library of vectors [phh3VL-VH-lib, see Fig. (**5b**)]. Because the VL and VH region genes, in each pair, are separated by *Sac* I and *Xho* I restriction enzyme sites, a cassette containing head-to-head bacterial promoter (P) and leader (*l*) sequences is obtained from vector #560 p*l*P*Zeo*P*l* [Fig. (**5b**)] and cloned between the *Sac* I and *Xho* I sites of phh3VL-VH-lib to drive expression of κ chain and Fd-cpIII (VH-CH1-cpIII) proteins. This generates a library of Fab phage display vectors [phh3-VL-*l*P*Zeo*P*l*-VH-lib, Fig. (**5c**)]. The bacterial promoter-leader cassette in vector #560 p*l*P*Zeo*P*l* had been generated from phagemid vector pComb3 [29], by a series of modifications [44,47]. The cassette contains the *lacZ* and *tac* promoters to drive expression of the κ and Fd-cpIII chains respectively. Although the leader sequences for both chains have the *pelB* leader amino acid sequence, the nucleotide sequences differ at many positions [44], and therefore, deletions are unlikely to occur during replication of the vector. The bacterial promoter-leader cassette also includes the selectable marker Zeocin™ [49,50] (driven by the synthetic promoter EM-7), which ensures that only vector molecules that have incorporated the cassette are perpetuated during library construction [47].

Transformation to produce colonies and infection of bacteria to produce phage display libraries are done as described [29]. The Fab phage display libraries can be selected for binding to polyantigens, to generate specific sublibraries (described in subsequent sections).

Mass Transfer of VL-VH Region Gene Pairs from the Phagemid Vector to a Bidirectional Mammalian Expression Vector

Generation of polyclonal whole antibodies requires the mass transfer of selected VL-VH region gene pairs from the phagemid vector to a mammalian expression vector, without loss of the VL-VH combinations. Therefore, a bidirectional mammalian vector for expression of mouse IgG2b antibodies was constructed ([43] and C.-Y. Kao and J. Sharon, manuscript in preparation). This vector, denoted #577 pMDV-IgG2b [Fig. (**6**), right side] contains the mouse γ2b heavy chain C gene and the mouse κ light chain C gene in opposite transcriptional orientations, as well as the *gpt* selectable marker, and mammalian transcription termination and polyadenylation sites.

VL-VH region gene pairs linked head to head (⟵⟶) in opposite transcriptional orientations, are transferred, in mass, between the (circular) bidirectional phage display vector and the (circular) mammalian expression vector. The transfer from a phage display to a mammalian expression vector requires opening the phage display vector with *Sac* I and *Xho* I [Fig. (**6a**)] between the VL and VH amino termini and replacing the prokaryotic *l*P*Zeo*P*l* cassette with a mammalian *l*PEHP*l*m cassette (which contains Ig promoter and leader sequences in opposite orientations as well a heavy chain enhancer), yielding the intermediate vector shown in Fig. (**6b**). The VL-VH pairs including

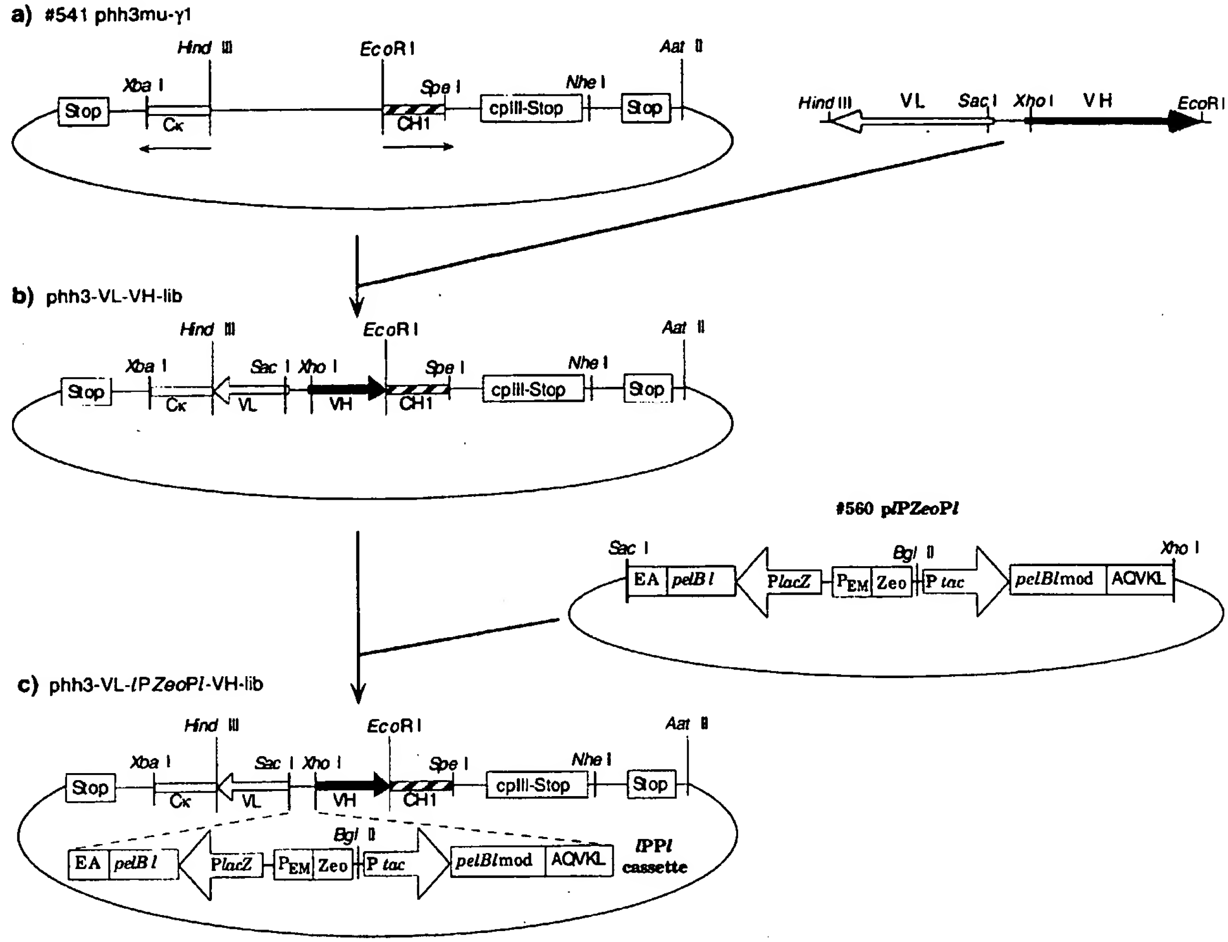

Fig. (5). Scheme for construction of Fab phage display libraries (partial maps and not to scale); all vectors are circular. The direction of transcription is indicated by arrows and by arrow heads on promoters and variable region genes

Symbols: P, promoter; *l*, leader sequence; *l*mod, leader sequence with modified nucleotide sequence; Stop, translation termination; *Zeo*, gene for Zeocin™ selectable marker. Amino acids encoded by the vectors are shown in one letter code.

the mammalian *l*PEHP*l*m cassette are then cut from the intermediate vector [Fig. (**6b**)] with *EcoR* I and *Hind* III and cloned into the *EcoR* I - *Hind* III sites of the pMDV-IgG2b mammalian vector, to generate pMDV-IgG2b-lib [Fig. (**6c**)]. (In the original design [44], the VL-VH region gene pairs including a mammalian promoter-leader cassette were lifted by PCR, and inserted into a mammalian vector. This step has subsequently been modified to use restriction enzyme-based transfer).

TESTING OF THE SYSTEM FOR GENERATING POLYCLONAL ANTIBODY LIBRARIES

The functionality of the bidirectional phage display and mammalian expression vectors as well as the generation and transfer of linked VL-VH region gene pairs were tested [43,44]. In one series of experiments [44], V region gene pairs derived from an A/J mouse that had been immunized with the hapten *p*-azophenylarsonate (Ars) coupled to keyhole limpet hemocyanin (KLH) were selected for Ars-binding in the phage display vector, transferred to the mammalian vector, and expressed as a mouse IgG2b PCAL. As expected, individual IgG2b antibodies from the PCAL had V region sequences and Ars-binding characteristics similar to those of anti-Ars hybridomas [44].

GENERATION OF POLYCLONAL FAB PHAGE DISPLAY LIBRARIES TO POLYANTIGENS

Using our system for PCAL generation, described above, we have generated Fab phage

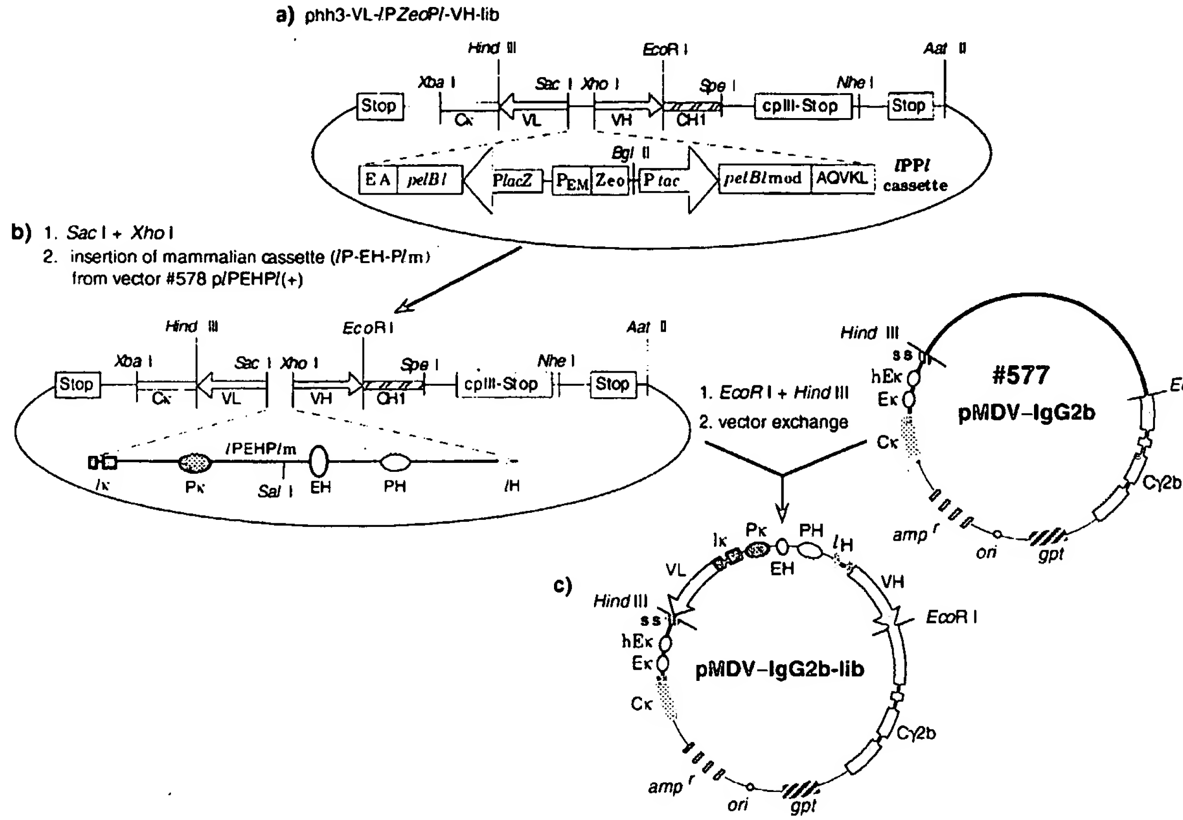

Fig. (6). Transfer of V region gene pairs between bidirectional phage display and mammalian expression vectors (partial maps and not to scale).

Symbols: Prokaryotic elements are as in Fig. (5). Mammalian regulatory elements are oval shaped. amp^r, ampicillin resistance; ori, prokaryotic origin of DNA replication; P, promoter; E, enhancer; *l*, leader sequence; ss, splice site; hum, human (all other mammalian regulatory elements are murine).

display libraries to infectious agents and cancer cells.

Generation of a Polyclonal Fab Phage Display Library to the Protozoan Parasite *Cryptosporidium parvum*

Cryptosporidium parvum is a protozoan parasite that causes severe disease in AIDS patients, for which there is no effective treatment [46]. A Fab phage display library was constructed from the RNA of spleen, intestine, nasopharynx, and bone marrow of *C. parvum*-immunized BALB/c mice. The Fab-displaying phage library was selected for binding to an oocyst/sporozoite preparation of *C. parvum*, generating an anti-*C. parvum* Fab phage display library of 5.2 x 10^4 members, which was tested for antigen-binding by direct ELISA. As shown in Fig. (7), the *C. parvum*-selected phage library bound to a *C. parvum*-coated plate whereas the unselected library and a negative control of phage containing the bidirectional phage display vector without the Fab gene sequences did not bind [46].

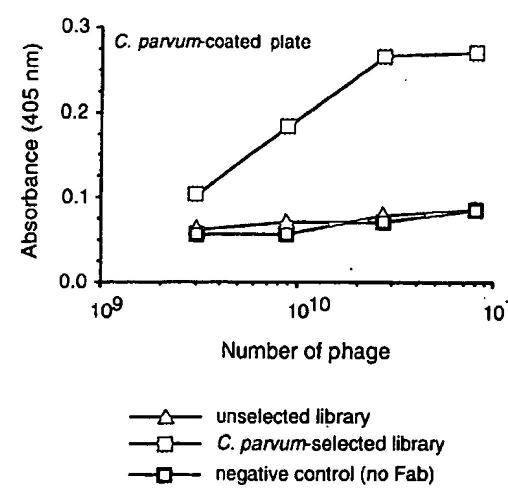

Fig. (7). Specificity of anti-*C. parvum* Fab phage display library shown by direct ELISA.

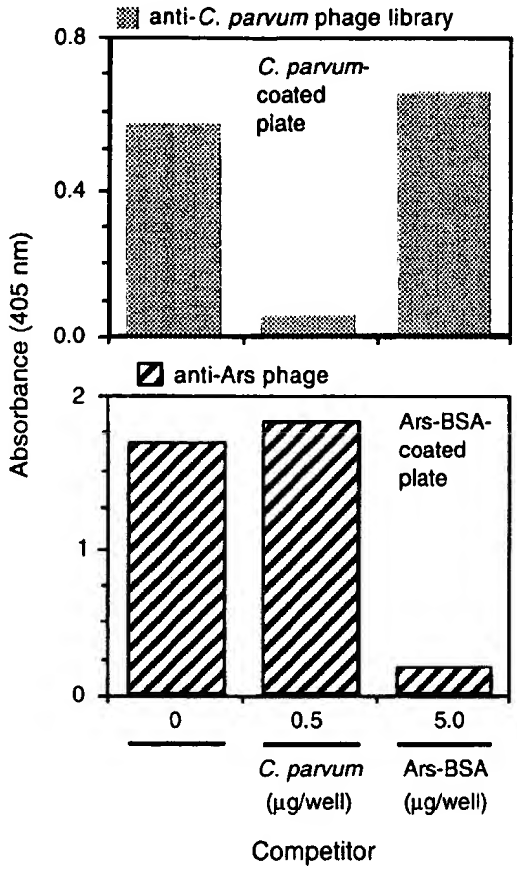

Fig. (8). Specificity of anti-*C. parvum* Fab phage display library shown by inhibition ELISA.

The specificity of the *C. parvum*-selected phage library was further demonstrated by a criss-cross inhibition ELISA using both the anti-*C. parvum*-selected phage and phage displaying Fab specific for the Ars hapten. As seen in the top panel of Fig. (**8**), the binding of the anti-*C. parvum* phage to solid phase *C. parvum* was inhibited by preincubation with the oocyst/sporozoite preparation but not by preincubation with Ars coupled to bovine serum albumin (BSA). Conversely, binding of the anti-Ars phage to solid phase Ars-BSA was inhibited by preincubation with Ars-BSA but not by preincubation with the oocyst/sporozoite preparation of *C. parvum* [see bottom panel of Fig. (**8**)].

Restriction fragment length polymorphism (RFLP) analysis and nucleotide sequencing of several members of the *C. parvum*-selected library indicated that the selected library is diverse.

Generation of Fab Phage Display Libraries to Human Ovarian Tumor Cell Membranes and Sheep Red Blood Cells

Cells from a surgically-resected human ovarian carcinoma (designated OC2), and sheep red blood cells (SRBCs) as control, were separately used to immunize mice [45]. BALB/c mice were immunized with either OC2 membranes or SRBCs by 3 intraperitoneal injections in complete Freund's adjuvant. RNA samples obtained from the spleens of the immunized mice were separately used to prepare Fab phage display libraries, using the system and primers described above. Each library was subjected to two consecutive pannings on wells coated with the immunizing polyantigen (OC2 or SRBC membranes, each library in two wells of a 24-well plate). Direct binding solid phase ELISA of the anti-OC2 and anti-SRBC Fab phage display libraries showed that successive panning increased specificity for the panning membranes [45]. Furthermore, binding of the second OC2 panned library to an OC2 membrane-coated plate was specifically inhibited by OC2 membranes but not by SRBC membranes. Conversely, binding of the second SRBC panned library to an SRBC membrane-coated plate was specifically inhibited by SRBC membranes but not by OC2 membranes [45].

Generation of a Fab Phage Display Library to the Human Breast Cancer Cell Line BT-20

A polyclonal Fab phage display library to BT-20 cells was constructed from RNA of spleen, bone marrow, and intestine from a BALB/c mouse that had been immunized with BT-20 cells [47]. To select an Fab phage sublibrary that reacts with the BT-20 carcinoma cells, phage were subjected to two consecutive rounds of panning on fixed BT-20 cells. The first pan yielded a library of 8×10^4 members, whereas the second pan yielded a library of 3×10^6 members. Analysis of the unpanned and panned Fab phage libraries by ELISA on fixed BT-20 cells showed that the second pan library binds better than the first pan library which, in turn, binds better than the unpanned library [47].

To confirm the specificity of the second pan Fab phage library for BT-20 cells, the library was tested in a criss-cross inhibition ELISA in conjunction with the panned anti-SRBC Fab phage library. BT-20 membranes inhibited the binding of the anti-BT-20 phage library to solid phase BT-20 cells in a

dose-dependent manner but not of the anti-SRBC phage library to solid phase SRBC membranes. Conversely, SRBC membranes inhibited the binding of the anti-SRBC phage library to solid phase SRBC membranes in a dose-dependent manner but not of the anti-BT-20 phage library to solid phase BT-20 cells [47].

RECENT LITERATURE ON SELECTION OF PHAGE DISPLAY ANTIBODY LIBRARIES TO MULTIANTIGEN TARGETS

Selection of phage displaying antibody fragments with desired antigen specificity, from a phage display antibody library with no demonstrable specific binding to the desired antigen(s), can be achieved by any method that separates antigen-binding phage from non-antigen binding phage. Commonly, antigen is immobilized on a solid surface and phage incubated with the antigen to capture binding phage, a method known as panning [29,33,51,52]. The solid surface is washed to remove non-binding phage, the binding phage are eluted and used to infect bacteria, resulting in amplification of the antigen-selected phage. Elution of bound phage can be achieved by any of several methods: using acidic solutions such as HCl-glycine [51], with basic solutions like triethylamine [33], by competition with antibodies to the antigen [53], or by enzymatic cleavage of a protease site engineered between the antibody fragment and the cpIII protein [54]. Alternatively, direct bacterial infection without chemical elution of phage has been used [55]. Sequential rounds of selection are often performed to obtain a high percentage of antigen-specific phage [29,33,51-53,55-65].

For selection of antibody-displaying phage (often referred to as "phage antibodies") to a multiantigen target (i.e. polyantigen), such as microbial or mammalian cells, panning as well as other methods have been used. Several groups have reported the successful isolation of phage antibodies binding to microbes by selecting on whole microbes [46,56,57,66]. Monolayers of adherent cancer cells and cell lines transfected to express an antigen of interest, either fixed [47,58-60] or non-fixed [39,61,62], have been used to successfully isolate specific phage antibodies. Many groups have also used such cell lines in suspension to select for binding phage [42,63-65,67-71]. The methods in which the phage antibodies that bind to the target cells are separated from the non-binders are diverse: centrifugation to pellet bound phage and target cells leaving non-binding phage in the supernatant [42,63-65], flow cytometry to isolate a specific cell population with bound phage [67,69,70], and magnetic beads to sort desired cell-binding phage [68,71]. Isolation of phage antibodies to cell surface antigens has also been reported by groups using cancer tissue sections on slides [72] and thymic tissue fragments [73].

These methods of selection are used to isolate binding phage (positive selection), however, one may wish to rid the library of phage antibodies that may cross-react with or have epitopes in common with another polyantigen (e.g. normal, non-cancerous cells). To achieve this one or more rounds of negative selection may be performed before or after positive selection, using normal cells (or any other polyantigen of choice) to absorb the unwanted cross-reactive phage antibodies [39,62,64]. A round of negative selection may be performed simultaneously with the positive selection by combining both positively selecting target cells (e.g. cancer cells) and negatively selecting absorber cells with the phage library, then separating the desired selecting target cells with binding phage from the absorber cells with binding phage [67,68]. Separation may be achieved with flow cytometry [67], magnetic beads [68], or any method to sort the target cells from the absorber cells. Once separated, only the phage bound to the target cells would be eluted.

There are many selection strategies one could use in the creation of polyclonal antibody libraries to polyantigens, as outlined above, but the strategy must be carefully designed because the composition of the output library of phage antibodies will depend on the method used. For example, one group's initial attempts to pan on confluent monolayers of transfected CHO cells yielded predominantly phage antibodies that were reactive with serum proteins. It was hypothesized that the serum proteins present in the cell culture medium adhered to the flask during cell growth and therefore were present during phage selection. The problem was overcome by a strategy that kept cells in suspension during selection [63].

In the same study it was also noted that as the number of selection rounds increased, the diversity of selected phage antibodies decreased, with certain clones dominating in later selection rounds [63]. The same problem was discussed at a recent antibody engineering conference, and it was pointed out that during selection procedures competition may cause loss of many potential

binders, resulting in output phage dominated by a few clones. This problem becomes even worse when using complex antigens such as whole cells. The presenting group solved the problem by doing only one round of selection [74]. Thus, for selection of polyclonal phage antibodies to polyantigens, it is especially important that the number of selection rounds be limited to one or two, as more selection rounds may restrict the size of the selected library.

CONCLUSION

The technology is now available for the production of polyclonal antibody libraries that will simultaneously recognize many epitopes on a multitude of antigens on tumor cells, microbes, or any other polyantigens, greatly reducing the chance of escape variants. These standardized antibody mixtures will be available in unlimited supply, will be amenable to alteration by genetic manipulations, and will be efficient at mediating effector functions to eliminate target polyantigens.

Regarding future FDA approval, PCALs should fall under the same category as such clinically used polyclonal antibody products as human gamma globulin preparations, anti-thymocyte globulin (ALG) and anti-thymocyte sera (ATS) [75,76]. Like these products, every PCAL batch will have to be tested for safety, but PCALs are expected to show much less batch-to-batch variability.

ACKNOWLEDGMENTS

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ABBREVIATIONS

Ars	=	*p*-Azophenylarsonate
BSA	=	Bovine serum albumin
C region or domain	=	Constant region or domain
H chain	=	Heavy chain
L chain	=	Light chain
PCAL	=	Polyclonal antibody library
PCR	=	Polymerase chain reaction
RT	=	Reverse transcription
SRBC	=	Sheep red blood cell
VH	=	Heavy chain variable region
VL	=	Light chain variable region

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Universal Antibody Libraries on Phage and Bacteria

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Combinatorial IgM Libraries

It is estimated that about 10^6–10^8 antibodies with different binding properties are present in the immune system at any one time. This number is sufficient to bind most antigens including synthetic compounds such as dinitrophenol that the immune system has never encountered. If it were thus possible to create antibody libraries with comparable numbers of truly diverse antibodies then it should be feasible to select an antibody from this library against any particular antigen.

A highly diverse antibody library can be obtained by amplifying and randomly combining chains of the naive IgM repertoire. These antibodies are expressed mainly on the surface of unactivated B lymphocytes. Attachment of antigen and interaction with T-helper cells then activates the B cell, which eventually matures into an IgG-secreting plasma cell. This process is accompanied by a somatic hypermutation of the antibody to increase its affinity for the antigen. In contrast to the employment of individual primers for each of the variable chain families [1, 2] we devised a strategy of minimal priming to generate a naive IgM library of more than 10^7 individual clones [3]. RNA from the peripheral blood lymphocytes of 20 donors was pooled prior to cDNA synthesis to reduce the relative amount of specific RNAs from any abundant B cell clones of individual donors. An average of 5×10^8 cells with a viability of >95% were prepared from each donor. The quality of the RNA was controlled by Northern blotting using a radioactively labelled oligonucleotide that hybridizes to the C-terminus of the constant region of human κ chains. The size of the generated cDNAs ranged up to 5 kb. About 1 μg of cDNA was used per polymerase chain reaction (PCR) amplification.

Given an average length of 1 kb, this amount contains 10^{12} cDNA molecules. Assuming that at least 1 mRNA out of 1,000 encodes for antibody chains in B cells (which represent >10% of the lymphocyte preparation), then at least 10^8 molecules of antibody cDNA were present in the starting material for each PCR. This corresponds to the number of different B cells used for the preparation. It is highly probable, therefore, that the complexity of the library is maintained during the preparation of antibody DNA.

We used backward primers homologous to the N-terminal part of the constant region instead of backward primers to the framework 4 region of the variable chain, as described by Marks et al. [1, 2] to reduce the effect of different primer affinities for each family of antibody DNA. Since the backward primers in our system are derived from highly conserved constant chain sequences, only the forward primers bear a risk of not priming a particular antibody DNA. In addition, the PCR conditions were optimized for the lowest possible hybridization temperature to enable priming from sequences with many mismatches. A meaningful statistical analysis of the variability is not possible, but partial sequencing of 19 individual clones of the κ sublibrary showed that 18 encode antibody DNA, and all these chains were different. The small proportion of nonantibody genes would appear to be quite acceptable as a consequence of achieving maximum variability.

The antibodies in this 'naive' library were expressed as single peptide chains after randomly combining the antigen-binding variable domains of κ or λ and μ chains. The peptide linker between the heavy and light chains consisted of approximately 18 amino acids containing an epitope recognized by the antitubulin monoclonal antibody YOL1/34. This enabled the antibodies to be easily identified on Western blots. For optimal production of the antibodies the antibody DNA was cloned into the antibody expression vector pOPE 90 [4].

It was often found that a significant percentage of the clones from antibody libraries that had been amplified by PCR from peripheral blood lymphocytes produced antibodies that were not in the expected size range. To reduce the number of these deletion mutants, we constructed the antibody expression vector pLAB in which DNA coding for a single-chain antibody was inserted into the gene encoding β-lactamase at the 3′-terminus of its signal sequence [5]. After transforming *Escherichia coli* with this vector, a fusion protein with a functional β-lactamase domain was produced that was able to protect the bacteria from the action of ampicillin. Libraries containing deletion mutants can therefore be usefully propagated with this vector, since only those inserts that are in frame with β-lactamase will survive.

Synthetic Gene Libraries

The most complex human antibody libraries could be achieved, in theory, by antibody gene synthesis employing random oligonucleotides for all the hypervariable regions [6]. In addition to completely novel structures and specificities, such libraries will not have been filtered through the negative selection process of the immune system. However, we are not employing completely random sequences for all the hypervariable regions, since statistically every antibody would then contain at least one stop codon. Furthermore, particular positions within the hypervariable regions are highly conserved and these have also been considered in designing the oligonucleotides.

At least five of the six hypervariable regions appear to consist of only a small repertoire of main chain conformations [7]. The CDR3 region of the heavy chain hypervariable regions, however, could not be classified into distinct known canonical structures. This is not surprising since the H3CDR region is the most variable. It also appears to make the largest contribution to the surface area available for contact with the antigen [8].

Substitution of the H3CDR region of a tetanus toxoid-binding Fab fragment with random sequences to create a semisynthetic library has demonstrated the potential of synthetic libraries for isolating novel specificities [9]. The randomization of the remaining five hypervariable regions, however, could conceivably create more problems than gains in the generation of highly diverse antibody libraries. If, for example, only particular sequence combinations can be accommodated in a restricted repertoire of canonical structures, then the chances of synthesizing an antibody with acceptable sequences in all six hypervariable regions are extremely low. On the other hand, these structures may just be reflecting the structural restraints imposed by the framework sequences and the more limited sequence variability in these regions than in H3CDR. It will therefore probably be necessary to systematically compare the quality of several synthetic libraries of antibodies containing an increasing number of restrictions in the randomness of each hypervariable region in order to choose conditions for obtaining the most diversity.

Vectors for Screening Antibody Libraries

For screening the highly diverse libraries mentioned above, that might contain at least 10^9 different antibodies, a method of clonal selection is required similar to that of the immune system in which the antibody is physically connected to its own gene [10]. This can be achieved by expressing the antibody on the surface of bacteria or bacteriophage. An excellent means

Universal A

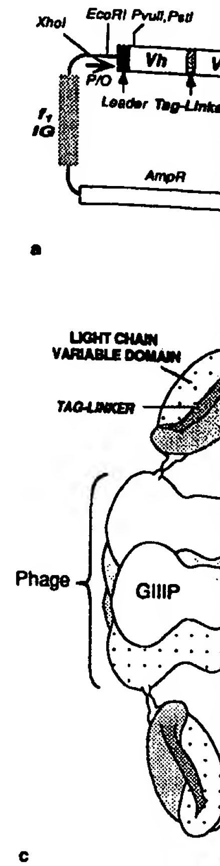

Fig. 1. Su
(a) phagemid pS
pAP1 [10] and *(c*
respectively. *Abb*
bacterial pectate
of an antilysozym
VL that include
trypsin cleavage
of the antibody
t_2 = transcription
region of phage f

: achieved, in ıucleotides for ›vel structures ;h the negative nploying com- ce statistically Furthermore, conserved and ›tides.
onsist of only ›R3 region of classified into ng since the ke the largest ıe antigen [8]. ŀ-binding Fab c library has novel specifi- iable regions, in the gener- nly particular repertoire of ıntibody with mely low. On he structural more limited will therefore ty of several ber of restric- ler to choose

'e, that might ıl selection is : antibody is by expressing cellent means

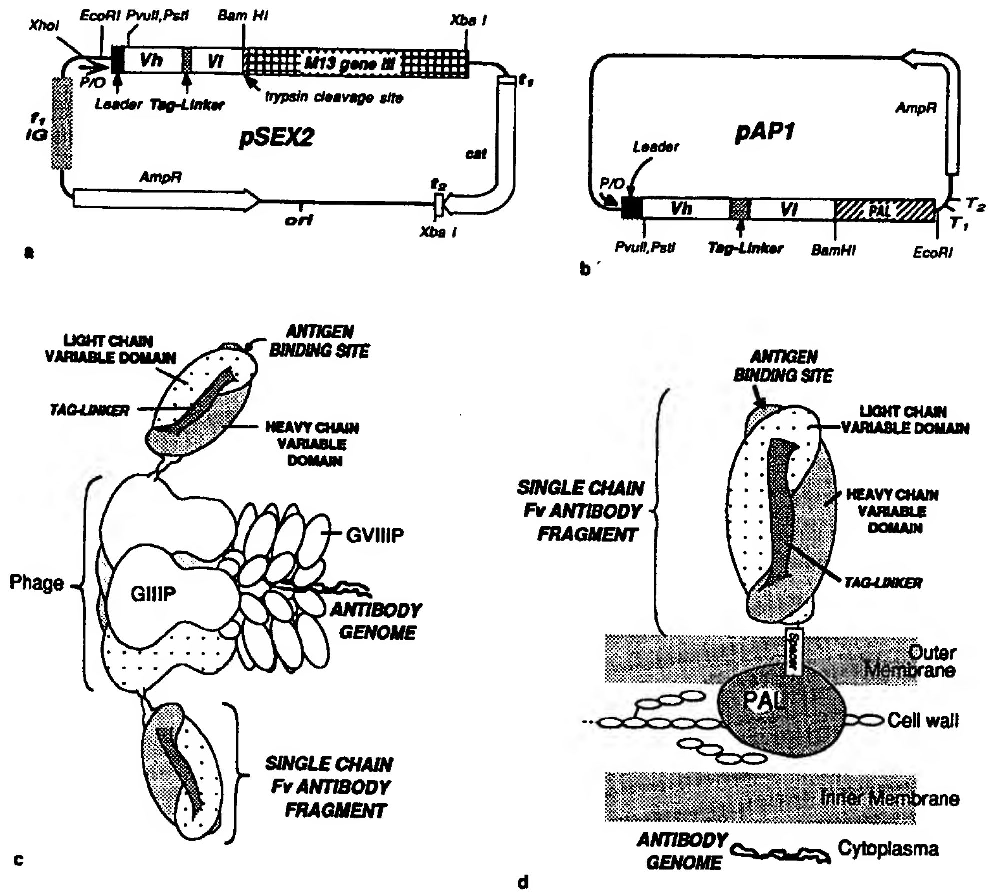

Fig. 1. Surface expression vectors for the display and screening of antibodies: *(a)* phagemid pSEX2 [14]; *(b)* antibody-peptidoglycan-associated protein expression plasmid pAP1 [10] and *(c, d)* artist's impression of antibody display obtained with pSEX and pAP1, respectively. *Abbreviations:* P/O = promoter/operator; Leader = signal peptide sequence of bacterial pectate lyase; VH and VL = heavy and light chain variable domains, respectively, of an antilysozyme antibody; Tag-Linker = oligo encoding 18 amino acids linking VH and VL that include an α-tubulin epitope recognized by the monoclonal antibody YOL1/34; trypsin cleavage site = LysAspIleArg. This optional sequence permits proteolytic cleavage of the antibody domains from pIII; cat = chloramphenicol acetyltransferase gene; t_1 and t_2 = transcription terminators; ori = origin of DNA replication for ColE1; f1 IG = intergenic region of phage f1.

of presenting polypeptides on bacteriophages is provided by the docking protein pIII of the M13 family of filamentous bacteriophages [11]. Peptides fused near to the N-terminus of pIII do not affect its function. Alternatively, fusions can be made with the C-terminal domain of pIII [12] using a phagemid vector and a helper phage to provide packaging proteins and wild type pIII. The relative amounts of wild type pIII and fusion protein can be adjusted so that only one of the three to five pIII sites is occupied by a fusion protein.

Various phage and phagemid systems have now been constructed for the expression of single chain Fv or Fab fragments fused to the N-terminus or C-terminal domain of pIII [13–16]. One advantage of phagemids as opposed to phages for antibody expression is that large amounts of DNA and antibody protein can be produced for analysis. The major consideration in our choice of a phagemid system, however, was the possibility to repress the production of the fusion protein when it is not required. This is particularly important during the amplification of antibody libraries since faster proliferating deletion mutants could quickly predominate. Using the antibody surface expression vector pSEX (fig. 1a, c), for example, the production of the antibody-pIII fusion protein in the absence of IPTG could not be detected in Western blots of bacterial lysates [14]. After induction with IPTG, large quantities of the fusion protein are then able to be produced, thus greatly facilitating its analysis. The fusion protein was identified by a monoclonal antibody to the tubulin epitope in the linker sequence between the heavy and light chains, and by antisera to their N-terminal sequences.

Bacterial surfaces would be more suitable for presenting high numbers of proteins and may provide an alternative means of screening antibody libraries. Using fluorescent tags, for example, it should be possible to isolate single cells expressing antibodies using a fluorescence-assisted cell sorter. Alternatively, magnetic beads or highly sensitive colony-screening assays could be used for selection. The latter procedure could prove to be particularly useful in the search for catalytic antibodies. To target antibodies to the surface of *E. coli*, we have fused a single chain Fv fragment to the N-terminus of the so-called peptidoglycan-associated lipoprotein [17] (fig. 1b, d). Immunofluorescence studies on unifixed cells showed that functional antibodies were accessible at the surface of intact bacteria. The applicability of this system for screening antibody libraries is presently being investigated.

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I Claim:

1. A library of receptor proteins expressed from a library of vectors wherein each vector contains a nucleic acid segment that encodes a pair of variable regions, which is contained in one of the receptor proteins, wherein the variable regions of each pair associate with each other to form a binding domain, and wherein the totality of nucleic acid segments in said library of vectors is diverse forming a library of polyclonal nucleic acid segments, wherein said library of polyclonal nucleic acid segments has been trans-

ferred in mass from a parent library of vectors to said library of vectors, wherein the vectors of said library of vectors have been modified, relative to the vectors of said parent library of vectors, by addition, subtraction, or substitution of coding sequences, and wherein said parent library of vectors has been selected in mass, for a subset of binding domains from a grandparent library of vectors, without characterization of all individual members of said grandparent library of vectors before said transfer from said parent library of vectors to said library of vectors without individual characterization of all members.

2. A library of recombinant receptor proteins wherein each receptor protein contains a pair of variable regions, wherein the variable regions of each pair associate with each other to form a binding domain, and wherein the totality of variable regions in said library of receptor proteins is diverse forming a library of variable regions, wherein said library of variable regions has been transferred in mass from a parent library of receptor proteins to said library of receptor proteins, wherein the receptor proteins of said library of receptor proteins have been modified, relative to the receptor proteins of said parent library of receptor proteins, by addition, subtraction, or substitution of sequences.

3. The library of claim **2** wherein said parent library of receptor proteins has been selected in mass, from a grandparent library of receptor proteins, for a subset of binding domains before said transfer from said parent library of receptor proteins to said library of receptor proteins.

4. The library of receptor proteins of claim **1**, **2** or **3** wherein said receptor proteins are specific for one or more antigens.

5. The library of receptor proteins of claim **1**, **2** or **3** wherein said receptor proteins are soluble proteins.

6. The library of receptor proteins of claim **1**, **2** or **3** wherein said receptor proteins are cell surface proteins.

7. The library of receptor proteins of claim **1**, **2** or **3** wherein said receptor proteins are antibodies of one or more isotypes selected from the group of isotypes consisting of IgG, IgM, IgA, IgE, and IgD.

8. The library of claim **7** wherein said antibodies are labeled with tags that facilitate detection and/or therapy.

9. The library of claim **8** wherein said tag is a radioactive molecule, toxic molecule, or enzyme molecule.

10. The library of claim **7** wherein said antibodies or parts thereof are derived from humans, mice, rabbits, or chickens.

11. The library of claim **7** wherein said antibodies are chimeric antibodies with variable regions derived from one species and constant regions derived from another species.

12. The library of claim **11** wherein said chimeric antibodies have murine variable regions and human IgG1 constant regions.

13. The library of claim **7** wherein said antibodies are truncated antibodies.

14. The library of claim **13** wherein said truncated antibodies are Fv fragments.

15. The library of claim **13** wherein said truncated antibodies are single-chain Fv fragments.

16. The library of claim **13** wherein said truncated antibodies are Fab fragments.

17. The library of claim **13** wherein said truncated antibodies are $F(ab')_2$ fragments.

18. The library of claim **7** wherein said antibodies have been further modified by mutagenesis.

19. The library of claim **7** wherein said antibodies are chimeric antibodies with antibody variable regions attached to enzymes, T cell receptors, or portions thereof.

20. The library of claim **19** wherein said antibody variable regions are attached to enzymes.

21. The library of claim **7** wherein said antibody variable regions are attached to T cell receptors or constant regions of T cell receptors.

22. The library of claim **1**, **2** or **3**, wherein the library of receptor proteins has been modified from said parent library of receptor proteins by said members having a constant region from a different species than the variable regions.

23. The library of claim **1**, **2** or **3**, wherein the library of receptor proteins is a library of antibodies, and wherein said library has been modified from the parent library by comprising whole antibodies.

* * * * *

-continued

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(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(i i) MOLECULE TYPE: DNA (genomic)

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(i i) MOLECULE TYPE: DNA (genomic)

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(B) TYPE: amino acid
(C) STRANDEDNESS: unknown
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(B) TYPE: amino acid
(C) STRANDEDNESS: unknown
(D) TOPOLOGY: unknown

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I claim:

1. A method for preparing a first library of expression vectors comprising paired nucleic acid fragments, said paired nucleic acid fragments being suitable for transfer to prepare a second library of different expression vectors, comprising the steps of:

(a) obtaining a plurality of nucleic acid fragments wherein each nucleic acid fragment encodes a variable region or part thereof of a protein which contains said variable region;

(b) producing a plurality of nucleic acid segments, wherein each segment comprises a pair of different nucleic acid fragments selected from said plurality of nucleic acid fragments and linked in opposite and divergent transcriptional orientations;

(c) cloning said plurality of nucleic acid segments into first circular vectors to produce a library of vector molecules;

(d) inserting a first cassette between the two nucleic acid fragments of each nucleic acid segment to produce a nucleic acid segment comprising said first cassette in a first library of expression vector molecules, wherein said first cassette contains at least one promoter ele-

ment permitting expression of said nucleic acid fragments in a first host cell;

(e) introducing said first library of expression vector molecules into the first host cells under conditions and time sufficient to express a first library of polypeptides, wherein each of the polypeptides contains a sequence encoded by one of said pairs of linked nucleic acid fragments; and

(f) isolating said first library of expression vector molecules from said first host cells.

2. The method of claim 1, which further comprises isolating the plurality of segments comprising said first cassette from said first library of expression vectors molecules, and inserting said plurality of segments comprising said first cassette into a plurality of second vectors to produce a second library of expression vector molecules.

3. The method of claim 1, which further comprises exchanging said first cassette from an expression vector of said isolated first library of expression vector molecules with a second cassette, wherein said second cassette contains at least one promoter element permitting expression of said nucleic acid fragments in a second host cell.

4. The method of claim 2, which further comprises exchanging said first cassette from an expression vector of said second library of expression vector molecules with a second cassette, wherein said second cassette contains at least one promoter element permitting expression of said nucleic acid fragments in a second host cell.

5. The method of claim 2, wherein said second library of expression vector molecules is introduced into a plurality of second host cells.

6. The method of claim 4, wherein the second vector is a circular vector.

7. The method of claim 5, wherein said first host cell is a prokaryotic cell and said second host cell is a eukaryotic cell.

8. The method of claim 5, wherein said first host cell is a eukaryotic cell and said second host cell is a second eukaryotic cell.

9. The method of claim 5, wherein said first host cell is a prokaryotic cell and said second host cell is a second prokaryotic cell.

10. The method of claim 5, wherein said first host cell is a eukaryotic cell and said second host cell is a prokaryotic cell.

11. The method of claim 1, wherein said protein is a secreted protein or receptor protein.

12. The method of claim 11, wherein the secreted or receptor protein is selected from the group consisting of an antibody and a T-cell receptor.

13. The method of claim 1, wherein one nucleic acid fragment of each segment of said plurality of nucleic acid segments encodes a heavy chain variable region of an antibody and the other nucleic acid fragment of the segment encodes a light chain variable region of the same antibody.

14. The method of claim 1 wherein said nucleic acid fragments comprise a polyclonal population encoding variable regions or portions thereof of proteins selected from the group consisting of antibodies, T-cell receptors, B-cell receptors, natural killer cell receptors, macrophage receptors and combinations thereof derived from a polyclonal cell population.

15. The method of claim 14, wherein the proteins are selected from antibodies or T-cell receptors.

16. The method of claim 1 wherein the first cassette contains two promoters in opposite transcriptional orientations.

17. The method of claim 3 wherein the second cassette contains two promoters in opposite transcriptional orientations.

18. The method of claim 1, wherein said first cassette further comprises a nucleic acid sequence encoding a leader sequence of a secreted protein or membrane protein, and said nucleic acid sequence encoding said leader sequence is operably linked to a nucleic acid fragment of said pair of nucleic acid fragments.

19. The method of claim 3, wherein said first cassette further comprises a nucleic acid sequence encoding a leader sequence of a secreted protein or membrane protein, and said nucleic acid sequence encoding said leader sequence is operably linked to a nucleic acid fragment of said pair of nucleic acid fragments.

20. The method of claim 1, wherein said first circular vector is a prokaryotic or eukaryotic surface display vector or expression vector.

21. The method of claim 2 wherein said second vector is a circular vector.

22. The method of claim 21, wherein said second circular vector is a prokaryotic or eukaryotic surface display vector or expression vector.

23. The method of claim 1 wherein said polypeptides of step (e) are antibodies.

24. The method of claim 23, wherein said antibodies are chimeric antibodies.

25. The method of claim 24, wherein said chimeric antibodies have mouse variable regions and human constant regions.

26. The method of claim 1, wherein step (f) includes a preliminary screening step to select desired expression vector molecules and thereby reduce the number of expression vector molecules used in preparation of said second library from those used in said first library.

* * * * *